

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
ACRYLONITRILE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**



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Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Acrylonitrile was identified as a priority compound for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing guideline in 1985. A review of the scientific and technical information relevant to setting an ambient air quality standard for acrylonitrile has previously been provided to stakeholders for their comments. This document provides the rationale for recommending Ambient Air Quality Criteria (AAQC) and a half-hour point of impingement (POI) standard for acrylonitrile.

Acrylonitrile is a colourless liquid with a faintly sweet and pungent odour. It is widely used as a chemical intermediate in a variety of industrial and commercial products and processes. Acrylonitrile does not occur naturally in the environment. It is produced industrially on a large scale and is emitted in large amounts in the form of vapours, and in aqueous effluents from facilities producing and using the chemical. Acrylonitrile is used as a raw material in the manufacturing of acrylic and modacrylic fibres, and in the production of plastics, and styrene-acrylonitrile, nitrile rubbers, nitrile barrier resins, adiponitrile, and acrylamide.

Acrylonitrile is not currently produced in Canada and is only used in the manufacturing of other products. According to occupational exposure and emission data, there appears to be greater exposure to humans and the environment from the use of acrylonitrile in end-user plants (3,000 to 20,000 $\mu\text{g}/\text{m}^3$) compared to production facilities (100 to 4,000 $\mu\text{g}/\text{m}^3$). Similarly, acrylonitrile levels around user plants are greater than around producing plants. The majority of acrylonitrile emitted is released into the air. According to the data reported in the National Pollutant Release Inventory (NPRI) of Environment Canada, one facility is responsible for nearly all releases in Ontario. The total reported atmospheric releases in Ontario for the years of 1993, 1994, 1995, 1996 and 1997, were 16.6, 17.6, 14.2, 8.9 and 5.2 tonnes, respectively. Acrylonitrile is not routinely monitored in Canada, however, ambient air monitoring results from the MOE Air Quality Study in Windsor indicates that acrylonitrile levels were below the detection limits which ranged from 0.21 to 0.64 $\mu\text{g}/\text{m}^3$.

Humans can be exposed to acrylonitrile through air, water and food. It is absorbed by the body through inhalation, oral, and to some extent dermal routes. The reported odour detection thresholds range from 8,000 to 50,000 $\mu\text{g}/\text{m}^3$. Exposure to acrylonitrile at concentrations of 7 to 45 $\mu\text{g}/\text{m}^3$ for 20 to 45 minutes leads to irritation of the mucous membranes, nausea, headaches and nervous irritability. Individuals also experience low grade anaemia, leukocytosis, kidney irritation and mild jaundice,

however, these effects subside when the exposure to acrylonitrile is terminated. Results have shown that children are more sensitive than adults.

Acrylonitrile is classified as a probable human carcinogen (class B1) by the United States Environmental Protection Agency (US EPA). This is based upon the observation of a statistically significant increase of lung cancer in humans and astrocytomas (cancer of non-neuron supportive cells) in the brain of rats. The International Agency for Research in Cancer (IARC) has classified acrylonitrile as a probable human carcinogen (group 2A) on the basis of sufficient evidence of carcinogenicity for animals, and limited evidence for humans.

Data from animal carcinogenicity studies indicated a significant dose-dependent increase in cancer incidence, and may provide support to the carcinogenicity in humans. Genetic toxicology studies showed acrylonitrile induced gene mutations in bacteria, yeast, and mammalian cells, sister chromatid exchange in mammalian cells, and cell transformation of three different cell types. On the basis of these results, acrylonitrile is considered a non-threshold carcinogen. The Toxicology Excellence for Risk Assessment (TERA) has recommended that the carcinogenicity of acrylonitrile in humans be reviewed based on more recent data. Under the CEPA (*Canadian Environmental Protection Act*), Environment Canada and Health Canada have recently completed a health and environmental assessment for acrylonitrile and consider that this compound is toxic and carcinogenic to humans.

The US EPA has established an inhalation cancer unit risk for lifetime exposure to acrylonitrile of 6.8×10^{-5} per ($\mu\text{g}/\text{m}^3$). That is, for a lifetime exposure to this chemical, at an ambient air concentration of $0.01 \mu\text{g}/\text{m}^3$, the probability of a cancer incidence is one in a million. Agencies, such as New Jersey, Massachusetts, Michigan and New York, have adopted the assessment and unit risk estimate from the US EPA to derive their long-term guidelines. California developed its own cancer unit risk estimate which resulted in a more conservative guideline. The WHO established its cancer unit risk estimate based on the same epidemiological study used by the US EPA but employed a different method of calculation which resulted in a unit risk of 2×10^{-5} per ($\mu\text{g}/\text{m}^3$). Environment Canada and Health Canada have derived a tumourigenic concentration at 5% increase in tumour incidence (TC_{05}) of $6 \text{ mg}/\text{m}^3$, based on data in female rats. In addition, several states have adopted the US EPA Chronic (non-cancer) Reference Concentration (RfC) of $2 \mu\text{g}/\text{m}^3$ as a benchmark for shorter averaging periods.

The current AAQC for acrylonitrile in Ontario is $100 \mu\text{g}/\text{m}^3$ for a 24-hour averaging time. The half-hour POI guideline is $300 \mu\text{g}/\text{m}^3$. Both criteria were established based on the protection of human health. In revising the air quality standards for Ontario, the Ministry of the Environment is reviewing and considering risk assessments, standards, and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, the Netherlands, the Swedish Institute of Environmental

Medicine and the Canadian Federal Government. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepts the scientific rationale and risk assessment employed by Environment Canada and Health Canada to develop their TC_{05} value of 6 mg/m^3 . The application of margin of safety factors of 5,000 and 50,000 to the TC_{05} produces risk concentrations of 1.2 and $0.12 \text{ } \mu\text{g/m}^3$, representing excess cancer risk of 1 in 100,000 and 1 in 1,000,000, respectively. The Ministry proposes to derive an annual AAQC based on the risk specific concentration of $0.12 \text{ } \mu\text{g/m}^3$.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for acrylonitrile:

- **an annual average AAQC of $0.12 \text{ } \mu\text{g/m}^3$ (micrograms per cubic metre of air) for acrylonitrile based on the carcinogenic effect of this compound; and,**
- **a 24-hour average AAQC of $0.6 \text{ } \mu\text{g/m}^3$ (micrograms per cubic metre of air) for acrylonitrile based on the carcinogenic effect of this compound.**

Based on supporting science and dispersion modelling, a half-hour POI standard of $1.8 \text{ } \mu\text{g/m}^3$ can be derived. However, considering the magnitude of the reduction from the current guideline of $300 \text{ } \mu\text{g/m}^3$ to this revised level of $1.8 \text{ } \mu\text{g/m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **$1.8 \text{ } \mu\text{g/m}^3$ to $180 \text{ } \mu\text{g/m}^3$ (micrograms per cubic metre of air) for acrylonitrile; these concentrations are equivalent to risk levels of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime, respectively.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

Table of Contents

Executive Summary	i
1.0 Introduction	1
2.0 General Information	3
2.1 Physical and Chemical Properties	3
2.2 Uses	4
2.3 Sources and Levels	4
2.4 Environmental Fate	5
3.0 Toxicology of Acrylonitrile	5
3.1 Acute Toxicity	6
3.2 Subchronic and Chronic Toxicity	7
3.3 Developmental and Reproductive Toxicity	7
3.4 Genotoxicity	7
3.5 Carcinogenicity	8
3.6 Environmental Effects	12
4.0 Existing Air Quality Criteria	13
4.1 Overview	13
4.2 Evaluation of Existing Criteria	16
5.0 Responses of Stakeholders to the Information Draft	21
6.0 Overview of the Next Phase of the Ministry's Standards Setting Process	21
7.0 Considerations in the Development of Air Quality Standards for Acrylonitrile	22
8.0 Recommendations	23
9.0 A Guide for Stakeholders Responding to this Posting	24
10.0 References	28
11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines	36
11.1 Agency-Specific Summary: Federal Government of the United States	36
11.2 Agency-Specific Summary: State of California	40

11.3	Agency-Specific Summary: State of Massachusetts	43
11.4	Agency-Specific Summary: State of Michigan	46
11.5	Agency-Specific Summary: State of New Jersey	48
11.6	Agency-Specific Summary: State of New York	50
11.7	Agency-Specific Summary: World Health Organization (WHO)	52
11.8	Agency-Specific Summary: The Netherlands	55
11.9	Agency-Specific Summary: Swedish Institute of Environmental Medicine	58
11.10	Agency-Specific Summary: Federal Government of Canada (CEPA)	59
12.0	Acronyms, Abbreviations and Definitions	62

1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

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- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Acrylonitrile was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the development of the existing guideline in 1985. A review of scientific and technical information relevant to setting an ambient air quality standard for acrylonitrile had been provided in a previous document, and was distributed to stakeholders for their comments. This document therefore provides the rationale for recommending AAQC and a POI standard for acrylonitrile.

2.0 General Information

2.1 Physical and Chemical Properties

Acrylonitrile is a volatile, flammable, colourless liquid with a faintly sweet, yet, pungent odour. The following list provides some of its properties:

CAS #	39447
RTECS #	AT5250000
UN #	UN1093
Conversion Factors	1 ppm = 2.17 mg/m ³ at 25 °C
Boiling Point	77.3 °C
Melting Point	-82 °C
Henry's Law Constant	8.8x10 ⁻⁵ atm-m ³ /mol
Flash Point	0 °C
Density	0.806 at 20 °C
Water Solubility	73,500 mg/L
Log K _{ow}	-0.07
Formula	C ₃ H ₃ N
Molecular Weight	53.1 g/mol
Vapour Density (air = 1)	1.9
Vapour Pressure	100 mmHg at 23 °C
Common Synonyms	acrylic acid nitrile, acrylon, carbacryl, cyanoethylene, 2-propenenitrile, vinyl cyanide

The odour detection threshold, as reported by the American Industrial Hygiene Association (AIHA) is 1.6 ppm (3400 µg/m³; this is also the geometric mean of air odour threshold). Similarly, the American Conference of Government Industrial Hygienists (ACGIH) states an odour threshold of 9,700 µg/m³. The Quebec Workplace Health and Safety Commission is in general agreement with the ACGIH, listing an odour detection limit at 8,000 µg/m³ (CSST, 1997). The odour detection threshold for acrylonitrile in air has been reported to be as high as 47,000 µg/m³ (Verschuere, 1983). The odour recognition thresholds have been reported to range from 3,700 to 50,000 µg/m³ (Cheminfo, 1996).

2.2 Uses

Acrylonitrile is widely used as a chemical intermediate in a variety of industrial and commercial products and processes. Acrylonitrile is used as a raw material in the manufacturing of acrylic and modacrylic fibres, and in the production of plastics and styrene-acrylonitrile, nitrile rubbers, nitrile barrier resins, adiponitrile, and acrylamide (ATSDR, 1990). It has been used as a fumigant for stored tobacco, flour milling and bakery food processing equipment; however, this practice has since ceased (IARC, 1979).

2.3 Sources and Levels

Acrylonitrile does not occur naturally in the environment (Howard, 1989). It is produced industrially on a large scale (WHO, 1986) and is emitted in large amounts. Emissions, which are generally in the form of vapours or aqueous effluents, are by-products of both the facilities that generate acrylonitrile, as well as those plants that use acrylonitrile in the production of other products. Acrylonitrile has been detected in cigarette smoke at levels of 1 to 2 mg per cigarette (IARC 1979; US EPA, 1983). It has also been detected in car exhaust, and may be released from polyacrylic fibers and plastics (Howard, 1989).

Since 1972, acrylonitrile has not been produced in Canada, however it is still imported (CEPA, 1999). All of the imported acrylonitrile comes from the U.S., and the amount has declined over the past two decades from 21,000 tonnes in 1976 to 7,600 tonnes in 1994 (CEPA, 1999). According to the National Pollutant Release Inventory (NPRI, 1993, 1994, 1995, 1996, 1997), on a national scale, on-site releases of acrylonitrile into the Canadian environment (air, water and soil) were 18.6, 19.5, 16.32, 10.84 and 5.19 tonnes, respectively. Almost all of these releases came from air emissions. The major source of releases was the organic chemical industries (97.4 %) (CEPA, 1999). For that same period, total reported releases to air for the province of Ontario were as follows: 1993 - 16.6 tonnes, 1994 - 17.6 tonnes, 1995 - 14.2 tonnes, 1996 - 8.9, and 1997 - 5.19 tonnes. One facility located in Sarnia, Ontario is responsible for most of these releases.

Acrylonitrile does not occur at measurable concentrations in the ambient air (US EPA, 1995). In general, the estimated level of human adult exposure to acrylonitrile via air from non-occupational exposure is below the detection limit. Acrylonitrile is not produced in Canada, however, in the US, acrylonitrile is produced industrially and is emitted in significant quantities from industrial sources. The estimated level of exposure to acrylonitrile of a population living within a 5 km radius of a chemical production factory or waste site is 2 to 12 $\mu\text{g}/\text{m}^3$ (ATSDR, 1990), while the level for those living near industrial plants that use acrylonitrile is 1 to 325 $\mu\text{g}/\text{m}^3$ (a). The estimated exposure to acrylonitrile of workers in an acrylonitrile factory is 100 to 4,000 $\mu\text{g}/\text{m}^3$ (ATSDR, 1990). In contrast, exposure to workers in an acrylic fibre plant is 3,000 to 20,000 $\mu\text{g}/\text{m}^3$ (US EPA, 1994a). In general, it appears that

acrylonitrile levels are higher around factories that use the raw acrylonitrile in the production of other products, rather than near those factories that produce acrylonitrile (US EPA, 1983).

Acrylonitrile is not part of routine ambient air monitoring programmes in Canada, and no ambient data could be obtained from federal sources (Dann, 1997). Atmospheric acrylonitrile concentrations, at various sites in and around Windsor, were monitored by the Ontario Ministry of the Environment and Energy in 1991 using real-time measurement methods (detection limit, approximately 0.21 to 0.64 $\mu\text{g}/\text{m}^3$). The results indicated that any acrylonitrile levels in the air were below the detection limits (MOEE, 1997).

The estimated ground level concentration (GLC) values for acrylonitrile were extracted from Ontario Ministry of the Environment's Certificates of Approval. From a sample of seven companies the median concentration was 0.17 $\mu\text{g}/\text{m}^3$, ranging from a minimum of 0.1 $\mu\text{g}/\text{m}^3$ to a maximum of 15 $\mu\text{g}/\text{m}^3$.

2.4 Environmental Fate

Acrylonitrile has a half-life in natural aquatic systems, primarily due to evaporation, ranging from 1 to 6 days, and secondarily due to biodegradation ranging from 6 to 21 days. In air, it is degraded primarily by photo-oxidation with a half-life of 9 hours to 9 days, depending upon atmospheric conditions. In soil, acrylonitrile evaporates rapidly or leaches into groundwater.

Environment Canada has determined that acrylonitrile has a Photochemical Ozone Creation Potential (POCP) of 25 which is considered moderate with regard to potential ozone formation (CEPA, 1999). However, actual contribution of photochemical ozone is dependent upon both reactivity and concentration of a substance. As acrylonitrile is only released from a few point sources within Canada and levels of acrylonitrile in ambient air within urban centres are generally below the detection limit of 0.9 $\mu\text{g}/\text{m}^3$, Environment Canada indicates that acrylonitrile causes only a very minor contribution to photochemical ozone formation (CEPA, 1999). Acrylonitrile is not expected to contribute to stratospheric ozone depletion and climate change (CEPA, 1999).

3.0 Toxicology of Acrylonitrile

The following toxicological review of acrylonitrile primarily focusses on the inhalation route of exposure, as this is the predominant pathway of human exposure, and since most of the released acrylonitrile is emitted to air. However, humans can also be exposed to acrylonitrile through, water and food, and it can enter the body by ingestion and to some extent via the dermal route (US EPA, 1983). Data on other exposure media are included in this document where relevant, or where inhalation data is lacking.

Acrylonitrile is absorbed rapidly after inhalation exposure. Within a few hours, approximately 40 - 50 % (exposed at 8.9 - 20 mg/m³) and 60 - 80% (exposed at 11 - 220 mg/m³) of the exposed concentrations have been found in the bodies of humans and animals, respectively (TERA, 1997). Absorption through the oral route is in the range of 90 - 98 % (TERA, 1997). Once absorbed, distribution through the body is rapid, with little potential for significant accumulation in any particular organ.

Acrylonitrile is metabolized by two major pathways which include, direct conjugation with glutathione, and oxidation by cytochrome P450 to 2-cyanoethylene oxide(CEO). 2-Cyanoethylene oxide is a mutagenic agent and alkylates DNA much more favourably than acrylonitrile (TERA, 1997; Woutersen, 1998). The CEO can be metabolized to cyanide, which may account for the acute toxicity of acrylonitrile. Acrylonitrile is detoxified through direct glutathione conjugation with acrylonitrile or with CEO. Species specificity in acrylonitrile metabolism has been reported between rats, mice and humans. More CEO is produced in mice than in rats and more CEO is metabolized to cyanide in mice. The kinetic parameters for rat and human microsomes were similar, and thus it was suggested that rats may be a good model species for the disposition of acrylonitrile for humans (TERA, 1997).

3.1 Acute Toxicity

Acute inhalation exposure to acrylonitrile may result in central nervous system effects such as headache, vertigo, nausea and convulsion (WHO, 1983; TERA, 1997). When humans are exposed to acrylonitrile concentrations of 7 to 45 µg/m³ for 20 to 45 minutes, they experience irritation of the mucous membranes, nausea, headaches and nervous irritability. (Wilson *et al*, 1948). Evidence suggests that acrylonitrile exposure may also induce alcohol intolerance and fatigue (Kaneko and Omae, 1992). Individuals also experience low grade anaemia, leukocytosis, kidney irritation and mild jaundice. These effects, however, subside when exposure to acrylonitrile stops (Wilson, 1944; Wilson *et al*, 1948). As is often the case, children are more sensitive to substances such as acrylonitrile than adults. In several instances, a child has died from inhalation of acrylonitrile vapour, whereas adults exposed to the same conditions experienced only minor irritations (ATSDR, 1990). The US Department of Health and Human Services calculated an acute (14-day) inhalation minimum risk level (MRL) of 1.5 ppm (3.15 mg/m³), based on a study (Jakubowski *et al*. 1987, as cited in ATSDR, 1990) showing neurological effects in workers.

In animals, observed LC₅₀ range from 300 - 990 mg/m³. Acute toxicity resembles cyanide poisoning which includes respiratory irritation and dysfunctioning of the central nervous system . (WHO, 1983; CEPA, 1999). Neurotoxicity following acute exposure develops in two phases. The first phase occurs shortly after exposure, likely due to the action of acrylonitrile, and resembles cholinergic over-stimulation, with effects such as vasodilation, extensive secretions such as the salivation, lacrimation, diarrhea and gastric secretion. The second phase is delayed by a few hours, likely caused by cyanide

toxicity, and manifested by central nervous disturbances such as trembling, ataxia, convulsions respiratory failure (TERA, 1997)

3.2 Subchronic and Chronic Toxicity

Chronic exposure can result in necrosis of the adrenal gland and the gastrointestinal tract, liver, kidney, lung and brain effects, dysfunctioning of the central nervous system and congestive lung oedema (TERA, 1997). A two-year study by Quast *et al.* (1980a, as cited in ATSDR, 1990) reported neurological effects (focal gliosis) and irritation of the nasal passage in rats exposed to 80 ppm (174 mg/m³). At this level of exposure no effects were noted in blood, liver or kidney.

Rats exposed to 10 mg/m³ acrylonitrile over 16 weeks had depressed T helper lymphocytes and T suppressor lymphocytes functions and diminished B lymphocyte transformation (Krivova *et al.*, 1982 as cited in WHO, 1983).

3.3 Developmental and Reproductive Toxicity

Murray *et al.* (1978, as cited in ATSDR, 1990 & WHO, 1983) exposed SD rats to 88,000 and 176,000 µg/m³ acrylonitrile vapour during the gestational period (6 to 15 days). The high dose group demonstrated a significant increase in foetal malformations. However, maternal toxicity was observed at both dose levels. Acrylonitrile teratogenicity was also demonstrated in hamsters resulting from intraperitoneal exposure on day 8 of gestation, with resulting malformations in the offspring (Willhite *et al.*, 1981 as cited in WHO, 1983).

Beliles *et al.* (1980 as cited in ATSDR, 1990) conducted a three-generation reproductive study on Charles River rats, administering acrylonitrile in drinking water. The results showed a reduction in both viability and lactation indices in the offspring as a result of maternal toxicity. Another study (Tandon *et al.*, 1988 as cited in ATSDR, 1990) suggests effects on male reproductive systems at 10 mg/kg/day.

3.4 Genotoxicity

Genotoxic properties of acrylonitrile are well documented and results have been mixed. In *in vitro* studies, acrylonitrile has elicited point mutations, clastogenic events, and has shown the ability to transform cells. Positive mutagenic responses have been observed in many genetic toxicology assays and on several phylogenetic levels from bacteria to humans.

Mutagenic activity was shown in prokaryotes (*Salmonella typhimurium* and *Escherichia coli*) and lower eukaryotes (*Saccharomyces cerevisiae*). A metabolic enzyme mixture was needed to elicit a mutagenic response with any strain of *Salmonella*, while *Escherichia coli* and *Saccharomyces*

cerevisiae produced positive results both in the presence or absence of metabolic enzymes (WHO, 1983). Gene mutations were also shown in cultures of mouse lymphoma L5178 TK+/- cells, and in human lymphoblasts at the thymidine kinase and 6-thioguanine loci hypoxanthine guanine phosphoribosyl transferase locus but not in Chinese hamster ovary (CHO) cells (CEPA, 1999). Both positive and negative results of sister chromatid exchange have been produced by acrylonitrile in both CHO cells and in human lymphoblasts in the presence of an activation system (TERA, 1997). Acrylonitrile induced sister chromatid exchange in human bronchial epithelial cells without the presence of S9 (TERA, 1997). Chromosome aberrations were observed in CHO cells by acrylonitrile in some *in vitro* studies (CEPA, 1999). Positive results have been observed in CHO cells in *in vitro* micronucleus assay studies (Woutersen, 1998). Acrylonitrile induced unscheduled DNA synthesis in primary rat liver hepatocytes but results were negative in human lymphocytes. Acrylonitrile induced DNA single-strand breaks in human bronchial epithelial cells, rat liver cells and calf thymus DNA (TERA, 1997). 2-Cyanoethylene oxide did not result in cell transformation of the *ras* oncogene in NIH3T3 cells (TERA, 1997).

Positive results have been observed in unscheduled DNA synthesis tests following administration of acrylonitrile by gavage in rats; however, results were negative in DNA repair and sister chromatid exchange in mice and rats following oral exposures (by gavage) (TERA, 1997). Except for an unscheduled DNA synthesis assay in rats, no mutagenic activity was observed *in vivo* either with chromosomal aberration or micronucleus assays in animal systems (Rabello-Gay and Ahmed, 1980).

Results of *in vitro* genotoxic studies with CEO were also mixed. Both positive and negative results have been observed in rat hepatocytes and rat HMEC. Positive results were reported for DNA single-strand breaks in calf thymus and pBR322 plasmid DNA (TERA, 1997). In two similar studies, CEO has been demonstrated to react with nucleotides of DNA *in vitro* to form adducts in TK6 lymphoblasts. It has been suggested that CEO induces DNA strand breaks and may interfere with DNA synthesis, and therefore may play a role in mutagenesis (TERA, 1997).

Recent genotoxic results of workers in a Hungarian Rayon plant, indicate that there may be *in vivo* genotoxic consequences in humans. The frequencies of chromosome aberrations, chromosome gaps and sister chromatid exchanges increased proportionally to the duration of exposure to acrylonitrile and/or dimethylformamide (Major et al., 1998). The fact that the factory air contained both acrylonitrile and dimethylformamide, raises some questions as to the impact of acrylonitrile by itself. However, this data does suggest a possible implication of acrylonitrile involvement.

3.5 Carcinogenicity

Long-term exposures to acrylonitrile through inhalation and oral routes have led to the development of tumours in animals. The common target organs are, the central nervous system (brain and spinal cord),

Zymbal gland, small intestine, forestomach and mammary gland (TERA, 1997). The data indicated a clear association between acrylonitrile exposure and cancer, with respects to, consistency in results from independent studies by different routes of exposure, positive dose-response indications for several tumour types and with statistically significant tumour incidences. The limitations of these studies are, only one species (i.e. rats) was studied and the predominant tumour types are rare in humans (e.g. astrocytomas in the brain, tumours in Zymbal gland and the forestomach).

Results obtained from epidemiological studies on exposed workers have been inconsistent. Increased mortality and/or incidence of lung and prostate cancers have been reported in some cohort studies whereas some follow-up studies and other studies do not provide similar results. Furthermore, two meta-analyses of combined data from 12 to 25 studies do not indicate an excess risk of mortality in exposed workers from all cancers, or specifically from respiratory cancer. The major deficiency in these human studies is the lack of reliable quantitative exposure data in dose-response assessment. The other confounding factor is that in most of the studies, there is a certain degree of co-exposure to other potential carcinogens (TERA, 1997; Collins and Acquavella, 1998).

In a retrospective epidemiology study of a fibers plant in the U.S. conducted by O'Berg (1980), 1,345 male textile workers exposed to low, medium and high concentrations of acrylonitrile, estimated as 11,000, 22,000 and 44,000 $\mu\text{g}/\text{m}^3$ were followed for more than 10 years. Twenty four cases of cancer were observed as compared with 19 expected. A significant increase in respiratory cancer was noted (e.g. 8 cases observed versus 4.1 expected), even when the contribution of smoking was taken into consideration (O'Berg, 1980). Three cases of prostate cancer were observed compared with 0.9 expected. There was an indication of increased cancer risk with increasing exposure duration. When a follow-up to the first study was published in 1985, again there was a marked increase in the number of lung cancer cases among those workers exposed to acrylonitrile (43 observed versus 36.7 expected) (O'Berg *et al.*, 1985). Though the increase in lung cancer incidence found in the follow-up study was not statistically significant, it found a significantly elevated prostate cancer rate (6 observed versus 1.5 expected).

In an analysis based on mortality, both the deaths related to the lung cancer and prostate cancer were statistically not significant. However, bladder cancer deaths were statistically significant, 3 observed versus 0.6 expected (O'Berg *et al.*, 1985). Results of a power analysis of the study suggest that, based on the size of the cohort, the study may not be sensitive enough to detect a significant increase in relative risk for lung cancer (O'Berg *et al.*, 1985; TERA, 1997).

Chen *et al.* (1987) studied 1,083 male workers at an acrylic fibers plant in the U.S. Potential exposure was classified into low, moderate and high exposure groups. In the high exposure group, there were 18 cancer deaths compared with 20.4 expected; of these, 5 were lung cancer deaths versus 7.6 expected. Based on exposure level or cumulative exposure index, no differences were observed between

observed and expected numbers. Four cases of prostate cancer were observed compared with 0.9 expected. This excess cancer risk was statistically significant and occurred in workers in the high exposure group, with over 20 years of exposure.

Male workers from two cohorts were studied for acrylonitrile exposures (Collins *et al.*, 1989). Four exposure categories were established based on industrial hygiene monitoring done in 1977 and assumed to represent levels at the plant start up. Exposures were defined as: none; 0.01 to 0.7 ppm/year (22 to 1500 $\mu\text{g}/\text{m}^3$ per year); 0.7 to 7 ppm/year (1500 to 15000 $\mu\text{g}/\text{m}^3$ per year); and >7 ppm/year (>15000 $\mu\text{g}/\text{m}^3$ per year). A total of 1774/2671 workers were considered exposed (i.e. a cumulative exposure of over 0.01 ppm/year). Forty three cancer deaths were observed with a standardized mortality ratio (SMR) of 1.01. Among these, 15 lung cancer deaths were reported (SMR = 1.0). Two deaths were from prostate cancer (SMR = 1.49). These results were similar to those of the non-exposed workers.

A retrospective cohort of eight companies in The Netherlands was studied by Swaen *et al.* (1992). Workers studied had exposures over 20 years. Exposure concentrations were estimated based on both an 8-hour time-weight-average and on job classifications: 0-0.5 ppm (0-1085 $\mu\text{g}/\text{m}^3$), 0.5-1 ppm (1085-2170 $\mu\text{g}/\text{m}^3$), 1-2 ppm (2170-4340 $\mu\text{g}/\text{m}^3$) and 2-5 ppm (4340-10850 $\mu\text{g}/\text{m}^3$). Peak exposures (<10 ppm, 10-20 ppm, 20-30 ppm) were also evaluated in this study. There were 42 observed cancer deaths compared with 50.8 expected; of these, 16 were trachea and lung cancer deaths compared with 19.5 expected and 2 prostate cancer deaths compared with 1.22 expected. In the non-exposed group, the SMR for all cancers and for cancers of the trachea and lung were similar to the those of the exposed cohort. However, for prostate cancer, there were 6 observed death compared with 10 expected in the non-exposed cohort. The authors suggested that acrylonitrile may not be a human carcinogen at concentrations occurred in the Dutch chemical industry.

Statistically significant increases in cancer incidence were also noted in two other epidemiology studies. Delzell and Monson (1982) noted a significant increase in lung cancer among rubber manufacturing plant workers, though exposure levels were not determined nor were smoking and exposure to other potential carcinogens taken into consideration. Thiess *et al.* (1980) observed a significant increase in lung and lymph system cancers in workers in a German acrylonitrile processing plant.

Werner and Carter (1981) reported an excess in total cancer deaths (stomach and lung cancers) among workers in an acrylonitrile polymerisation and acrylic fibre spinning plant, but the increase was not statistically significant. In contrast to the findings of these studies, seven other studies reported no evidence of carcinogenic risk from acrylonitrile exposure (WHO, 1983). All of the studies, however, suffer from inadequate consideration of the variables, methodological difficulties, or inadequate exposure information regarding acrylonitrile or other carcinogens (WHO, 1983; 1987). Four recent epidemiological studies from cohorts in the U.K., The Netherlands and the U.S.A. did not establish a

causal relationship between occupational acrylonitrile exposure and increased cancer mortality (Benn and Osborne, 1998; Blair *et al.*, 1998; Swaen *et al.*, 1998; Wood *et al.*, 1998). Most of these studies suffer from limiting factors which have been experienced in previous studies. These limitations include, a lack of information on workers' smoking habits, limited estimates of acrylonitrile exposure and relatively small size of the cohorts (Benn and Osborne, 1998; Swaen *et al.*, 1998; Wood *et al.*, 1998). In the study performed by the National Cancer Institute, even though workers smoking habits were factored in, exposure concentration was monitored and a rather large number of acrylonitrile plants involving over 25,460 workers were also included, such causal relationship was still not observed (Blair *et al.*, 1998). In a few situations, a higher, but not statistically significant lung cancer mortality was observed. However, there was no consistent trend to establish a dose-response relationship (Benn and Osborne, 1998; Blair *et al.*, 1998).

There are only a few inhalation studies available to assess the carcinogenicity of acrylonitrile in animals. A detailed two-year inhalation carcinogenicity study was conducted in Sprague-Dawley rats (100/sex/group) exposed to 0, 20, 80 ppm (0, 44,000 and 174,000 $\mu\text{g}/\text{m}^3$) of acrylonitrile for 6 hours/day, 5 days/week for two years (Quast *et al.*, 1980a). Non-neoplastic effects observed included inflammatory and degenerative changes in the nasal turbinates and the central nervous system. These changes were particularly prevalent and more intense in the 80 ppm group and likely attributed to the irritation of acrylonitrile. Statistically significant increases in tumour incidence were noted in male and female rats. The tumours observed were those of the central nervous system (astrocytomas; statistically significant for the 20 and 80 ppm dose groups), Zymbal gland (statistically significant for the 80 ppm group only), tongue (statistically significant for the 80 group only), small intestine (statistically significant for the males in the 80 ppm group only), and mammary gland (only if adenocarcinoma was considered for the increase; no difference between control and exposed animals was observed if all mammary tumours were considered). Some animals were exposed to acrylonitrile for a little less than two years because animals had to be sacrificed due to the appearance of large mammary gland tumours (ATSDR, 1990; US EPA 1983; US EPA, 1999a). In addition, in a long-term carcinogenicity bioassay, Maltoni *et al.* (1988) observed tumours in the liver of rats. There are no data in the literature for an inhalation bioassay performed in a species other than the rat.

Similar results of statistically significant increases in tumour incidence were observed following treatment of Sprague-Dawley and Fischer 344 rats to acrylonitrile by the oral route of exposure (Quast *et al.* 1980b; Biodynamics, 1980).

Caution should be exercised when attempting extrapolation of the predominant acrylonitrile-induced CNS tumour (astrocytoma) incidence which has occurred in rats to humans (TERA, 1997). No acrylonitrile-related excess brain cancer risk was reported in any of the epidemiology studies. In fact, brain cancer deaths were reported to be lower in the exposed than in the non-exposed groups in some studies (Collins *et al.*, 1989; Swaen *et al.*, 1992; Wener and Carter, 1981). In a retrospective study

of mortality in workers exposed to acrylonitrile in various industries in The Netherlands, slightly higher brain cancer deaths were found; however, no brain tumour deaths were noted in the high exposure group (Swaen *et al.*, 1998). The absence of a dose-effect characteristic argues against a causal relationship between brain tumour death and acrylonitrile exposure. It has been suggested that humans have a pathway for the detoxication of acrylonitrile which is absent in rodents, and this may render humans to be less sensitive to acrylonitrile carcinogenicity than animals (TERA, 1997). As well, acrylonitrile carcinogenicity has not been reported in animal species other than the rat. However, there are no data available to suggest that acrylonitrile-induced tumourigenic events do not occur in other animal species.

Based on the consistence in acrylonitrile-induced cancer incidences in rats, a clear causal relationship exists between exposure and the various types of tumours through both oral and inhalation routes of exposure, possible mutagenic effects of acrylonitrile and its oxidative metabolite (2-cyanoethylene oxide) in both human and rat tissues. In addition a causal relationship does exist between available human carcinogenicity data for increased lung and prostate cancer mortality in some cohorts, though these increases are not dose-related and do not reach a statistically significant level. Therefore, the carcinogenic potential of acrylonitrile to humans cannot be ruled out.

Considering sufficient evidence in animals and some evidence in humans, various agencies have classified acrylonitrile as a potential carcinogen. The US EPA (1999) considers acrylonitrile to be a probable human carcinogen (class B1) based on the observation of a significant increase in the incidence of lung cancer in exposed workers and on the observation of tumours in rats exposed either by inhalation or oral routes. The International Agency for Research on Cancer (IARC) also classified acrylonitrile as a probable human carcinogen (group 2A) based on sufficient evidence for animals, but with limited carcinogenic evidence for humans. The ACGIH (1991) has given acrylonitrile a suspected human carcinogen classification on the basis of carcinogenicity in animals with data showing relevance to worker exposure, and conflicting or insufficient epidemiological studies for cancer in exposed humans.

3.6 Environmental Effects

Toxicity data for wildlife species are not available in the literature. Studies of 13 insect species found that LC_{50} values for these insects ranged from 1.1×10^5 to $3.7 \times 10^7 \mu\text{g}/\text{m}^3$ (CEPA, 1999). A fifty percent decrease in progeny was reported in rice weevil (*Sitophilus oryzae* L.) as the result of 8-hour exposures to $4.0 \times 10^5 \mu\text{g}/\text{m}^3$ acrylonitrile (Rajendran and Muthu, 1981). The rice weevil was the most sensitive of the insect species studied as 4-hour exposures to 1×10^6 to $1.5 \times 10^6 \mu\text{g}/\text{m}^3$ acrylonitrile resulted in 100% mortality (Rajendran and Muthu, 1977).

Environment Canada reviewed numerous aquatic toxicity studies for its Priority Substances List Assessment Report of acrylonitrile and concluded that acrylonitrile was moderately toxic to fish and amphibians as 96-hour LC_{50} values range from 10 to 20 mg/L (CEPA, 1999). The US EPA has not set criteria for the protection of aquatic life. It reports an acute lowest effect concentration (LEC) in freshwater organisms of 7.6 mg/L and a chronic LEC of 2.6 mg/L. A 28-day study in bluegill sunfish showed a half-life of 4 to 7 days.

Studies conducted in China on the toxicity of acrylonitrile to duckweed (*Lemna minor* L.) determined a 96-hour no-observed-effect concentration (NOEC) of 6.2 mg/L and a 96-hour lowest-observed-effect concentration (LOEC) of 12.5 mg/L for inhibition of plant growth (Zhang, 1997).

Acrylonitrile concentrations of up to 5,000 mg/L do not appear to be toxic to bacterial species as acrylonitrile is readily degraded (Wenzhong et al, 1991). Applications of 1,000 $\mu\text{g/g}$ acrylonitrile to soil were found to affect soil microbes as decreased soil respiration was observed over a monitoring period of 6 days (Walton et al, 1989).

4.0 Existing Air Quality Criteria

4.1 Overview

The current Ontario 24-hour Ambient Air Quality Criterion (AAQC) for acrylonitrile is 100 $\mu\text{g}/\text{m}^3$ and the half-hour point of impingement (POI) guideline is 300 $\mu\text{g}/\text{m}^3$. The basis for both criteria was protection of human health (MOEE, 1994a).

In revising the air quality standards for Ontario, the Ministry of the Environment is considering risk assessments, and standards and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, the Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. Agency specific summaries of information guidelines for acrylonitrile are presented in Section 11.0 of this report. A brief summary is presented in Table 1.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment normally uses a factor of 15 to convert from criteria, based on annual average concentrations to half-hour POI standards and a factor of 3 to convert from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term

exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Most of the agencies reviewed have developed long-term ambient air quality criteria with basis based on the carcinogenic and non-carcinogenic properties of acrylonitrile.

The US EPA has established an inhalation cancer unit risk of 6.8×10^{-5} per ($\mu\text{g}/\text{m}^3$) for lifetime exposure to acrylonitrile. That is, for a lifetime exposure to this chemical at an ambient air concentration of $0.01 \mu\text{g}/\text{m}^3$, the probability of a cancer incidence is one in a million. Agencies, such as, New Jersey, Massachusetts, Michigan and New York have adopted the assessment and unit risk estimate from the US EPA to derive their long-term guidelines. California developed its own cancer unit risk estimate which resulted in a more conservative guideline. The WHO established its cancer unit risk estimate based on the same epidemiological study used by the US EPA, but employed a different method of calculation and resulted in a unit risk of 2×10^{-5} per ($\mu\text{g}/\text{m}^3$).

The US EPA has also developed an inhalation reference concentration (RfC) of $2 \mu\text{g}/\text{m}^3$ based on lung cell hyperplasia in rats. The states of California, Massachusetts, Michigan and New Jersey have adopted the RfC of the US EPA for their criteria derivation. The short-term guideline concentration of the State of New York was derived from the occupational exposure limits developed by the US National Institute for Occupational Health and Safety (NIOSH).

Table 1. Summary of Existing Air Quality Guidelines¹ for Acrylonitrile

Agency	Guideline Value ²	Basis of Guideline	Date ³	Comments
USEPA (IRIS)	2 µg/m ³ (inhalation reference exposure level)	2-yr rat inhalation, Lung cell hyperplasia	1991	LOAEL (HEC) adjusted with uncertainty factors
	0.01 µg/m ³ (lifetime exposure)	Lung cancer in humans	1992	1*10 ⁻⁶ additional cancer risk
	0.1 µg/m ³ (lifetime exposure)	unit risk 6.8 x 10 ⁻⁵ per µg/m ³		1*10 ⁻⁵ additional cancer risk
California (CAPCOA)	1 µg/m ³ (lifetime exposure)			1*10 ⁻⁴ additional cancer risk
	2 µg/m ³ (chronic annual)	Respiratory and skin irritation	1993	Non-cancer Reference Exposure Level (Chronic annual); IRIS
Massachusetts	0.003 µg/m ³ (lifetime exposure)	Lung cancer in humans	1996	1*10 ⁻⁶ additional cancer risk
		unit risk 2.9 x 10 ⁻⁴ per µg/m ³		
Michigan	0.4 µg/m ³ (24-hour average)	Lung cell hyperplasia	1995	Threshold and non-threshold effects
	0.01 µg/m ³ (lifetime exposure)	Lung cancer in humans	1991	1*10 ⁻⁶ additional cancer risk
New Jersey		unit risk 6.8 x 10 ⁻⁵ per µg/m ³		
	2 µg/m ³ (24-hour average ITSL)	Lung cell hyperplasia	1991	Screening level for a 24-hour averaging time
New York	0.01 µg/m ³ (lifetime exposure)	Lung cancer in humans	1987	Annual average IRSL; US EPA
		unit risk 6.8 x 10 ⁻⁵ per µg/m ³		
WHO	2 µg/m ³ (annual average)	Lung cell hyperplasia	1994	Ambient annual guideline concentration, annual average
	0.01 µg/m ³ (lifetime exposure - based on IRIS)	Lung cancer in humans	1994	1*10 ⁻⁶ additional cancer risk; US EPA carcinogen class: B1
The Netherlands		unit risk 6.8 x 10 ⁻⁵ per µg/m ³		
	220 µg/m ³ (1-hour average - SGC)	Occupational exposure limits	1994	Acute 1-hour average; based on NIOSH REL-TWA
Sweden	0.01 µg/m ³ (annual - AGC)	Lung cancer in humans	1994	Chronic annual; 1*10 ⁻⁶ additional cancer risk; US EPA
		unit risk 6.8 x 10 ⁻⁵ per µg/m ³		
Canada (CEPA)	0.05 µg/m ³ (lifetime exposure)	Lung cancer in humans and rats	1987	1*10 ⁻⁶ unit cancer risk
	0.5 µg/m ³ (lifetime exposure)	unit risk 2 x 10 ⁻⁵ per µg/m ³		1*10 ⁻⁵ unit cancer risk
Ontario	1 µg/m ³ (Annual average)	Basis not available	1992	Basis not available
	0.1 µg/m ³ (lifetime exposure)	Basis not available	1992	1*10 ⁻⁶ additional cancer risk (target value)
Ontario	none		1993	No value found
	0.12 µg/m ³ (lifetime exposure)	TC ₀₅ of 6000 µg/m ³ divided by 50000 and 5000 respectively	1999	PSL2 assessment based on TC ₀₅ of 6000 µg/m ³ for female rats
Ontario	1.2 µg/m ³ (lifetime exposure)			
	100 µg/m ³ (24 hour average)	Health	1994	24-hour averaging time: Ambient Air Quality Criteria
Ontario	300 µg/m ³ (POI; half-hour))	Health	1985	Point Of Impingement guideline

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations
- As different jurisdictions use different units to express concentration, when necessary a conversion factor of 1 ppm = 2203 µg/m³ was used.
- Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

The Netherlands uses its MIC (Maximum Immission Concentration) of $1 \mu\text{g}/\text{m}^3$ as an annual average limit value for acrylonitrile by applying a factor of 1000 for carcinogens to the MAC (Maximum Acceptable Concentration), and adjusting for the odour threshold with a factor of 10. It has also set as a long-term target value of $0.1 \mu\text{g}/\text{m}^3$ for lifetime exposure.

Environment Canada and Health Canada have listed acrylonitrile as a priority chemical (PSL2) for risk assessment under the *Canadian Environmental Protection Act* (CEPA, 1999). A Tumourigenic Concentration at a 5% increase in incidence or mortality (TC_{05}) of $6 \text{ mg}/\text{m}^3$ has been proposed. The application of a margin of safety factor of 5000 and 50000 will provide protection to that is comparable to the range for low dose risk estimates generally considered by various agencies to be “essentially negligible”, i.e. 10^{-5} and 10^{-6} respectively (Health Canada, 1996).

Workplace exposure limits have been established by different agencies. The Occupational Safety and Health Administration (OSHA) has set the legal airborne PEL-TWA (Permissible Exposure Limit - Time Weighted Average) at $4,400 \mu\text{g}/\text{m}^3$ over an 8-hour work shift, and the ceiling, or the limit not to be exceeded during any 15-minute work period, at $22,000 \mu\text{g}/\text{m}^3$. The NIOSH has set a REL-TWA (Recommended airborne Exposure Limit - Time Weighted Average) of $2,200 \mu\text{g}/\text{m}^3$, and $22,000 \mu\text{g}/\text{m}^3$ as the limit not to be exceeded during any 15-minute work period (NIOSH 1994, 1988b). The American Conference of Governmental Industrial Hygienists (ACGIH) has set a TLV-TWA (Threshold Limit Value - Time Weighted Average) at $4,400 \mu\text{g}/\text{m}^3$ (ACGIH, 1991). Acrylonitrile also carries an OSHA and ACGIH skin notation, as dermal exposure can result in systemic effects. The US Department of Health and Human Services calculated an acute (14-day) inhalation minimum risk level (MRL) of 1.5 ppm ($325 \text{ mg}/\text{m}^3$), based on a study showing neurological effects in workers (Jakubowski et al. 1987, as cited in ATSDR, 1990).

4.2 Evaluation of Existing Criteria

Most of the acute effects of acrylonitrile exposure resemble symptoms of cyanide poisoning, such as the CNS effects of headache, nausea, vertigo and convulsion and effects of the liver. Acute exposure of rats induces irritation caused directly by acrylonitrile, and respiratory effects by cyanide poisoning resulting from the breakdown of CEO. Most of the agencies reviewed do not have criteria developed based on the acute effects of acrylonitrile. The short-term criteria of New York was derived from an occupational exposure limit (TLV-TWA), whereas the 24-hour ITSL of Michigan was adopted from the chronic RfC of the US EPA.

Information on the adverse systemic effects of long-term or chronic exposure to acrylonitrile was primarily obtained in studies designed for carcinogenicity bioassays. Except the inflammatory changes observed in the nasal turbinates, non-cancerous changes observed generally involved the hyperplastic alterations in the CNS and the respiratory epithelium. Furthermore, neurophysiological changes in

motor and sensory conduction have also been reported. Other systemic effects include necrosis of the adrenal gland and the gastrointestinal tract, liver, kidney, lung. Most of the U.S. agencies adopted the RfC developed by the US EPA for their long-term non-carcinogenic air quality guidelines. All the agencies reviewed consider the acrylonitrile-induced cancer effect as the most sensitive endpoint and have developed carcinogenicity-based air quality guidelines. The approaches of developing air quality standards based on carcinogenic and non-carcinogenic effects will be examined in the following.

Criteria Based on Carcinogenicity

In general, all the U.S. agencies reviewed have adopted or derived their values from the inhalation lifetime cancer risk estimate developed by the US EPA (US EPA, 1999a). The data used for the estimate was obtained from the retrospective cohort epidemiology study for increased lung cancer incidence in humans (O'Berg, 1980). Male textile workers, exposed to low, medium and high concentrations, estimated as 11,000, 22,000 and 44,000 $\mu\text{g}/\text{m}^3$ of acrylonitrile, were followed for at least 10 years. A significant increase in respiratory cancer was noted, even when the contribution of smoking was taken into consideration (O'Berg, 1980).

The US EPA used the average relative risk model to calculate the inhalation unit risk of $6.8 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$; a lifetime exposure to 0.01 $\mu\text{g}/\text{m}^3$ of acrylonitrile is estimated to result in an additional cancer risk to humans of 1 in 1,000,000. The US EPA considers that the cohort in the study of O'Berg (1980) was sufficiently large and was followed for an adequate period. A dose-response relationship for the increased cancer risk was observed. Furthermore, the increased risk remained after adjustment for smoking. The exposure levels of 5 to 20 ppm (11 to 44 mg/m^3) were estimated by company representatives (US EPA, 1999a).

The US EPA has also derived an inhalation cancer unit risk of $1.5 \times 10^{-5} \cdot (\mu\text{g}/\text{m}^3)^{-1}$ based on the animal data of Quast, *et al.* (1980a). This cancer unit risk is within an order of magnitude of the unit risk estimate based on the human data of the study of O'Berg (1980). This finding appears to lend support to the carcinogenic classification for acrylonitrile. However, the significance of tumours found in experimental animals is unknown. For example, some tumour incidences in animals include those located in the Zymbal gland and the forestomach, two anatomical features not found in humans.

Using the same rationale used by the US EPA, Massachusetts, Michigan, New Jersey, and New York consider 0.01 $\mu\text{g}/\text{m}^3$ to be their annual exposure limit. California modified the US EPA unit risk to the upper 95% bound, and considered 70 years rather than 60 years for the duration of exposure. This resulted in a unit risk of 2.9×10^{-4} per $\mu\text{g}/\text{m}^3$ acrylonitrile. That is, exposure to 0.003 $\mu\text{g}/\text{m}^3$ would result in an estimated one in a million excess cancer risk (OEHHA, 1997a).

The WHO (1987) considers acrylonitrile as if it were a human carcinogen based on its carcinogenicity in animals because of the limited evidence of carcinogenicity in humans. Using the average relative risk model, a value for unit risk was determined to be 1.7×10^{-5} per ($\mu\text{g}/\text{m}^3$) for acrylonitrile (WHO, 1987).

The WHO (1987) found this value consistent with the lifetime inhalation risk derived from animal studies in the 1983 US EPA Health Assessment Document. The WHO does not recommend a safe level for acrylonitrile, and concludes that at $1 \mu\text{g}/\text{m}^3$ the lifetime risk is about 2×10^{-5} . This represents an additional cancer risk to humans of 1 in 1,000,000 over a lifetime exposure to $0.05 \mu\text{g}/\text{m}^3$.

Acrylonitrile has elicited genotoxic properties in several *in vitro* and *in vivo* studies using animal and human tissues. Furthermore, toxicologists at TERA suggested that non-carcinogenic effects of acrylonitrile do not appear to be a prerequisite for the carcinogenic toxicity of this compound (TERA, 1997). Therefore, acrylonitrile is considered to be a non-threshold carcinogen by both the US EPA and the IARC, and more recently by TERA and the Canadian federal government.

The lack of a clear human carcinogenicity picture has led toxicologists at the Toxicology for Excellence in Risk Assessment (TERA) to suggest that acrylonitrile's human carcinogenic classification must be re-evaluated as the current classification may no longer be supportable (TERA, 1998). The TERA has decided to employ data from an animal inhalation study to derive its cancer risk slope factor for acrylonitrile. Their reasoning for this is based on: results from epidemiological studies are equivocal; available human studies have methodological limitations, such as a lack of reliable exposure information and co-exposure to other potential carcinogens; the power of these studies is low to detect a statistically significant cancer risk in exposed workers; and the results of meta-analyses of data from many epidemiological studies did not indicate a causal relationship between occupational exposure to acrylonitrile and subsequent death from respiratory cancer. On the other hand, animal data provide a consistence of acrylonitrile-induced cancer incidences in the rats and a clear causal relationship between exposure and the various types of tumours through both oral and inhalation routes of exposure (TERA, 1997).

The inhalation study of Quast *et al.* (1980a) was chosen as the primary source of data. In the absence of a biologically-based model to extrapolate experimental exposure concentrations to human equivalent exposure concentrations, as recommended by the US EPA in its recently Proposed Guidelines for Carcinogen Risk Assessment (US EPA, 1996), the methods developed by the US EPA to calculate human equivalent concentrations (HEC) in the derivation of the reference concentration (RfC) was used. The human equivalent concentrations of 0, 7.5 and $30 \text{ mg}/\text{m}^3$ were derived from the exposure concentrations of 0, 20 and 80 ppm in the animal study. Of the four target organs examined, analysis has been focussed on the modelling of the astrocytomas, which have the most consistent occurrence across studies and exposure routes. The Zymbal gland is not a comparable target organ in humans, and tumours of the tongue and the small intestine were not observed by the oral route of exposure.

The astrocytoma data have been adjusted for early mortality (this was not indicated in the US EPA's assessment based on the same study), and a linear extrapolation (polynomial model) method has been employed to perform the analysis. Based on the US EPA's proposed guidelines (US EPA, 1996) the ED₁₀ (effective dose at 10% increase in tumour incidence) was calculated to be 14.55 and 12.18 mg/m³ and the LED₁₀ (95% lower confidence limit of the ED₁₀) to be 9.09 and 9.11 mg/m³ for the male and the female rats respectively. Accordingly, the slopes (slope = 0.1 / ED₁₀ or LED₁₀) were calculated to be 0.0069 per mg/m³ ($6.9 \times 10^{-6} \cdot (\mu\text{g}/\text{m}^3)^{-1}$) and 0.0082 per mg/m³ ($8.2 \times 10^{-6} \cdot (\mu\text{g}/\text{m}^3)^{-1}$) based on ED₁₀ and, 0.011 per mg/m³ and 0.011 per mg/m³ ($1.1 \times 10^{-6} \cdot (\mu\text{g}/\text{m}^3)^{-1}$) based on the LED₁₀ for the male and female rats, respectively. The risk specific concentrations (calculated as excess risk = slope x [acrylonitrile] in mg/m³) for the female were slightly greater than those of the male rats. It was determined that for the female rats, based on the ED₁₀, the risk specific concentrations were:

10⁻⁴ risk: 12 µg/m³
10⁻⁵ risk: 1.2 µg/m³
10⁻⁶ risk: 0.12 µg/m³

based on LED₁₀, the risk specific concentrations were:

10⁻⁴ risk: 9 µg/m³
10⁻⁵ risk: 0.9 µg/m³
10⁻⁶ risk: 0.09 µg/m³.

The TERA suggests that this cancer potency may represent an overestimation of actual risk to humans (TERA, 1997) because: it is considered that the astrocytoma is rare in humans; the conversion of an intermittent exposure dosage to continuous regime also results in an overestimation of risk; and the detoxication mechanism for acrylonitrile in humans may be more efficient than rodents and this renders humans to be less sensitive than animals to acrylonitrile carcinogenicity.

Acrylonitrile is listed as a priority chemical (PSL2) for risk assessment under CEPA (CEPA, 1999). In agreement with most agencies reviewed, Environment Canada and Health Canada consider cancer the critical endpoint for quantitative dose-response risk assessment. The inhalation study of Quast *et al.* (1980a) has been chosen as the key source for quantitative data and astrocytoma of the CNS has been considered the most appropriate tumour type for cancer risk estimation. Environment Canada and Health Canada consider that acrylonitrile-induced carcinogenesis may not be unique to rats and suggest that based on PB-PK modelling predictions, cyanoethylene oxide in the brains of humans would be considerably higher than those in rats exposed to similar concentrations of acrylonitrile. The lack of evidence of brain tumours in epidemiological studies may be attributable to the limited power to detect the excess of rare brain tumours (CEPA, 1999). In their assessment, both benign and malignant

tumours of the astrocytoma type in the CNS were combined for the calculation, using a multistage model (GLOBAL 82). Tumour incidences have been adjusted to exclude animals dying before six months (prior to observation on the first tumour). Dose scaling between animals and humans was considered because of the difference in inhalation volume and body weight, based on the averaged breathing volume of 0.11 m³ air/day for a 0.35 kg rat and 23 m³/day for a 70 kg adult human.

The tumourigenic concentration at 5% increase in incidence or mortality (TC₀₅) for the combined tumour incidence of tumours in the brain and the spinal cord in female rats is estimated to be 6000 µg/m³ (8900 µg/m³ for the male rats). This is the lowest TC₀₅ (human equivalent value). The lower 95% confidence limit is 4500 µg/m³. The application of a margin of safety factor of 5000 and 50000 to the TC₀₅ will provide protection that is associated with the range for low dose risk estimates generally considered by various agencies to be “essentially negligible”, i.e. 10⁻⁵ and 10⁻⁶ respectively (Health Canada, 1996). Thus, at an exposure concentration of 1.2 µg/m³ for a lifetime, the likelihood of tumour incidence is one in a hundred thousand. This value is in close agreement with the risk specific concentration at an equivalent risk level based on the ED₁₀ for female rats as estimated by TERA.

Criteria based on non-cancer end points

The non-carcinogenic end-point for injury to the nasal respiratory epithelium in rats, based on the inhalation study of Quast *et al.* (1980a), was employed by the US EPA to calculate a Reference Concentration (RfC) of 2 µg/m³ for acrylonitrile. Sprague-Dawley rats were exposed to 0, 44,000 or 174,000 µg/m³ of acrylonitrile for two years. A dose-dependent, and statistically significant increase in degenerative and inflammatory changes in the respiratory epithelium and nasal turbinates was observed with the acrylonitrile-treated animals. The RfC was calculated from an inhalation LOAEL-HEC (Lowest Observed Adverse Effect Level - Human Equivalent Concentration) by the application of a total uncertainty factor of 900: 10 for the protection of sensitive individuals; 3 to adjust from a minimally adverse LOAEL to a NOAEL; 3 for interspecies variability; and 10 for deficiencies in the database). The overall confidence in the RfC was given as medium to low. Though the study on which the RfC was based was well conducted, it involved only one species and it did not identify a NOAEL. There are a lack of chronic or subchronic data in a second species, and a lack of reproductive data via inhalation, while an oral study showed reproductive effects.

Michigan and New Jersey have adopted the US EPA RfC of 2 µg/m³ for their air quality criteria based on a 24-hour average period. California has adopted the US EPA RfC as its chronic reference exposure Level (REL).

New York (1994) classifies acrylonitrile as a contaminant with high toxicity. It derived a Short-term Guideline Concentration (SGC; 1-hour) of 220 µg/m³ by applying an uncertainty factor to the REL-TWA of 2,200 µg/m³ of the NIOSH. NIOSH (1988,1997) notes that since acrylonitrile is a potential

carcinogen, the REL-TWA of 1 ppm (2,200 µg/m³) is based on the lowest feasible concentration. The US Department of Health and Human Services calculated an acute (14- day) inhalation minimum risk level (MRL) of 1.5 ppm (3250 µg/m³) based on a study showing neurological effects in workers (Jakubowski et al. 1987, as cited in ATSDR, 1990).

5.0 Responses of Stakeholders to the Information Draft

In January, 1999 the Ministry posted information draft documents for eighteen chemicals, including acrylonitrile, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies that the Ministry has considered appropriate for the development of air quality standards; the appropriateness of considering the carcinogenicity of acrylonitrile as the most sensitive endpoint; and, any technical or economic impacts that may be anticipated as a consequence of the potential revision(s) of the air quality standard.

During the consultation period the Ministry received three submissions from various stakeholders regarding the draft document for acrylonitrile. A rubber industry stakeholder commented that it would be possible to meet a revised standard at a value of an order of magnitude (10-fold) lower than that of the current interim POI standard and further reductions may be achieved by applying additional control technology. Comments from a utility stakeholder indicated that the release of acrylonitrile from their facility was almost negligible. One federal government agency suggested that, where possible, information regarding the releases and uses of acrylonitrile specific to Canada and Ontario should be used.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard is now complete. During this initial phase stakeholders were also encouraged to provide additional information such as any technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed ambient air quality criteria and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for acrylonitrile. If the proposed standard cannot be achieved immediately, this phase will be followed by a third phase in which risk management options will be

discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder inputs regarding the economic impacts and technical feasibility of achieving the standard. In the meantime, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds. For instance, where there is a greater than 10-fold difference between the revised health-based values and the current standard, an interim standard may be warranted depending on the extent of risk management analyses.

7.0 Considerations in the Development of Air Quality Standards for Acrylonitrile

The current Ambient Air Quality Criterion (AAQC) for acrylonitrile in Ontario is 100 µg/m³ for a 24-hour averaging time. The half-hour POI guideline is 300 µg/m³. These criteria were established based on the adverse health effects of acrylonitrile.

Inhalation of acrylonitrile through acute exposures may result in central nervous system effects such as headache, vertigo, nausea, and convulsion. In animals, acute inhalation exposure may induce toxicity resembling cyanide poisoning which includes respiratory irritation, inflammatory and degenerative changes in the respiratory epithelial tissues, as well as central nervous systems dysfunction. Chronic exposure induces necrosis to liver, lungs, kidney, the central nervous system and respiratory tissue damage. All six of the U.S. agencies reviewed have developed air quality criteria based on the adverse effects of acrylonitrile on respiratory tissues.

There is evidence that acrylonitrile may be genotoxic. This is supported by positive mutagenic assay results observed in some bacteria, animal and human cells *in vitro*, despite *in vivo* study results which are less consistent. It is also suggested that non-carcinogenic effects of acrylonitrile do not appear to be a prerequisite for the carcinogenic effect of this compound.

The most sensitive endpoint of chronic acrylonitrile exposure is the development of cancer. In rats, it has been consistently demonstrated that chronic exposure to acrylonitrile through the inhalation and oral routes induces cancer. Tumours in the brain, spinal cord, and Zymbal gland are the most common tumour types found in rats. Results from human studies based on available epidemiological data are less consistent as the Zymbal gland is not found in humans, as such, similar brain tumours have not been reported in workers at acrylonitrile plants. Lung and prostate cancers have been found to be associated with exposure to acrylonitrile in workers in some cohorts. Unfortunately, follow-up studies always fail to confirm the significance of these findings. The major deficiency in these human studies is the lack of reliable quantitative exposure data in dose-response assessment. Furthermore, in these studies, workers were often co-exposed to certain other carcinogens that existed in the plant.

In spite of the uncertainties in the data concerns about the carcinogenic potential of acrylonitrile have led to the development of cancer-based exposure limits by most agencies. These agencies suggest that exposure to air concentrations of acrylonitrile in the range of 0.003 to 0.12 $\mu\text{g}/\text{m}^3$ over a lifetime may result in an additional cancer risk of one in a million.

The scientific rationale and the risk assessment for the TC_{05} of Environment Canada and Health Canada are supported by a recent independent risk assessment performed by TERA and by a group of panel toxicologists of TERA. Thus, the TC_{05} is considered the most appropriate basis for the development of air quality standards for acrylonitrile in Ontario. The application of margin of safety factors of 5,000 and 50,000 to the TC_{05} produces risk concentrations of 1.2 and 0.12 $\mu\text{g}/\text{m}^3$, respectively. These values are in close agreement with the risk-specific concentration of 1.2 and 0.12 $\mu\text{g}/\text{m}^3$ (at lifetime exposure cancer risk levels of one in a hundred thousand and one in a million, respectively), derived based on the ED_{10} for female rats, as estimated by TERA.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide and the science upon which these standards are based. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepts the scientific rationale and risk assessment employed by Environment Canada and Health Canada to develop their TC_{05} values for the tumourigenic (tumour causing) effect of acrylonitrile. The application of margin of safety factors of 5,000 and 50,000 to the TC_{05} produces risk concentrations of 1.2 and 0.12 $\mu\text{g}/\text{m}^3$, representing excess cancer risk of 1 in 100,000 and 1 in 1,000,000, respectively.

In general, the Ministry strives to manage exposure to carcinogens down to a risk represented by no more than 1 excess cancer in 1,000,000. This is consistent with the Ministry's approach to carcinogenic risk management for other environmental exposures (e.g., drinking water and contaminated sites) and with other jurisdictions, in particular throughout the United States. As a result, the Ministry proposes to derive an annual AAQC based on the risk specific concentration of 0.12 $\mu\text{g}/\text{m}^3$.

The Ministry of the Environment normally uses a factor of 15 to derive half-hour POI standards and guidelines from criteria based on annual average concentrations and a factor of 3 to derive POIs from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements which ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b).

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for acrylonitrile:

- **an annual average AAQC of $0.12 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for acrylonitrile based on the carcinogenic effect of this compound; and,**
- **a 24-hour average AAQC of $0.6 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for acrylonitrile based on the carcinogenic effect of this compound.**

Based on supporting science and dispersion modelling, a half-hour POI standard of $1.8 \mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current guideline of $300 \mu\text{g}/\text{m}^3$ to this revised level of $1.8 \mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **$1.8 \mu\text{g}/\text{m}^3$ to $180 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for acrylonitrile; these concentrations are equivalent to risk levels of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime, respectively.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the

submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of

cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, "*Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998*" may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE *Guideline F-14 (formerly 02-01), "Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects" Economic Services Branch- April 1994*, and;

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- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards." Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>*

Comments relevant to the setting of air quality standards for acrylonitrile can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* US Environmental Protection Agency

3. *Guideline Value(s):*

No ambient air exposure limits are currently promulgated. The reference concentration for chronic inhalation exposure (RfC) is $2 \mu\text{g}/\text{m}^3$ (US EPA, 1999a; last review 08/15/91).

Acrylonitrile is classified as a probable human carcinogen (B1) with a unit risk from inhalation exposure of 6.8×10^{-5} per $(\mu\text{g}/\text{m}^3)$.

4. *Application:*

IRIS was developed as a source of consistent risk information on chemicals for use in decision-making and regulatory activities. However, values derived and presented in IRIS do not represent guidelines on their own. IRIS also contains a summary of current American government regulatory actions under various mandates.

5. *Documentation Available:*

US EPA, 1999a. Integrated Risk Information System (IRIS) Database. On-line. US Environmental Protection Agency. Office of Research and development, Washington, D.C., U.S.A.

Key Reference(s):

Beliles, R.P., H.J. Paulin, N.G. Makris and R.J. Weir. 1980. Three-Generation Reproductive Study of Rats Receiving Acrylonitrile in Drinking Water. Prepared by Litton Bionetics, Inc., Kensington, MD, for the Chemical Manufacturers Association, Washington, DC.

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US EPA. 1983. Health Assessment Document for Acrylonitrile. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC.

Werner, J.B. and J.T. Carter. 1981. Mortality of United Kingdom Acrylonitrile Polymerisation Workers. Br. J. Ind. Med. 38: 247-253.

6. Peer Review Process and Public Consultation:

US EPA makes use of peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, both within the EPA and within other science-based US regulatory agencies. Information is put on IRIS after results of the public review and comments on draft documents/information have been addressed.

7. Status of Guideline:

No current guidelines exist for acrylonitrile.

8. Key Risk Assessment Considerations:

The US EPA (1999) has calculated an RfC which represents risk from adverse effects other than cancer. This RfC was calculated using results from a 2-year rat inhalation study (Quast *et al.*, 1980). Rats were exposed to 0, 7,700 and 31,000 µg/m³ of acrylonitrile for 6 hours/day, 5 days/week for 2 years. In the high dose group, a statistically significant increase in mortality was noted in the first year for rats of both sexes. In the lower dose group, female rats were sacrificed early due to the occurrence of

large, benign, mammary gland tumours. This sacrifice during the last 10 weeks of the study was due to an increase in the onset, occurrence and size of spontaneously occurring tumours. Gross and histopathological evaluation showed exposure-related adverse effects to the nasal respiratory epithelium and the brain. The incidence of glial cell tumours (astrocytomas) was significantly increased in both male and female rats at the high dose level (31,000 $\mu\text{g}/\text{m}^3$). The NOAEL(HEC) and the LOAEL(HEC) for non-carcinogenic, extra-respiratory effects are 7,700 $\mu\text{g}/\text{m}^3$ and 31000 $\mu\text{g}/\text{m}^3$, respectively. An inhalation uncertainty factor of 1000 (10 for the protection of unusually sensitive individuals; 3 for the adjustment from a minimally adverse LOAEL to a NOAEL; 3 for interspecies variability, and 10 due to an incomplete database, specifically, the lack of inhalation data in a second species) was used to arrive at the RfC of 2 $\mu\text{g}/\text{m}^3$. The inhalation RfC is rated medium in confidence predominantly because it was based on a study using only one species.

For the cancer risk assessment, the average relative risk dose extrapolation method was used to calculate a unit risk from inhalation exposure of 6.8×10^{-5} per $\mu\text{g}/\text{m}^3$ based on results from O'Berg (1980). This is equivalent to an estimated excess cancer risk of 1 in 10^6 for lifetime exposure to 0.01 $\mu\text{g}/\text{m}^3$ of acrylonitrile.

Several epidemiology studies have examined the morbidity and mortality of workers exposed to acrylonitrile. In the O'Berg (1980) study, a trend of increased cancer incidence was noted with duration of exposure and increased length of follow-up time. All but one of the cancer cases were respiratory and occurred with 6 or more months of exposure. Some other studies have been performed but they all suffer from inadequate study design or methodology. Significant increases in lung cancer incidence among rubber manufacturing plant workers were noted (Delzell and Monson, 1982). Thiess *et al.* (1980) noted an increase in lung cancer and cancer of the lymph system in acrylonitrile processing workers. Werner and Carter (1981) noted a statistically significant increase in stomach and pulmonary cancer among workers in the polymerisation of acrylonitrile and the spinning of acrylic fibers. Quast *et al.* (1980) and Maltoni *et al.* (1977) exposed Sprague-Dawley or Fischer rats, respectively, to acrylonitrile and showed statistically significant, usually dose-dependent, increases in tumours of the central nervous system (astrocytomas), Zymbal gland, stomach, tongue, small intestine and/or the mammary gland. Developmental studies showed a significant increase in offspring with malformations as well as a decrease in the litter size (Beliles *et al.*, 1980).

9. Key Risk Management Considerations:

None, since no guidelines for ambient air exist.

10. Multimedia Considerations of Guidelines:

The oral drinking water unit cancer risk for acrylonitrile is reported at 1.5×10^{-5} per ($\mu\text{g}/\text{L}$). The oral slope factor was calculated as 0.54 per (mg/kg)/day. The ambient water quality criteria for freshwater aquatic organisms show the acute LEC to be 7,550 $\mu\text{g}/\text{L}$ and the chronic LEC to be 2,600 $\mu\text{g}/\text{L}$.

11. *Other Relevant Factors:*

The US EPA (1999) gives a medium confidence to its chronic RfC: Medium confidence in the study because only one animal species was used and no NOAEL was observed, and medium confidence in the database due to lack of chronic and sub chronic data in a second species and lack of inhalation reproductive studies when oral studies show reproductive effects.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* State of California (Office of Environmental Health Hazard)

3. *Guideline Value(s):*

The chronic inhalation reference exposure level for acrylonitrile is $2 \mu\text{g}/\text{m}^3$ and has been adopted from the US EPA. A unit cancer risk factor of 2.9×10^{-4} has been adopted, which is equivalent to $0.003 \mu\text{g}/\text{m}^3$ at 1 in 10^6 excess cancer. Acrylonitrile is listed as a substance requiring the calculation of annual average concentration. Chronic exposure reference levels should be compared with modelled annual average air concentrations.

4. *Application:*

"The intent of the Committee in developing the guideline was to provide risk assessment procedures for use in the Air Toxics 'Hot Spots' program." (CAPCOA, 1993). This program is based on a California State Law, the Air Toxics 'Hot Spots' Information and Assessment Act of 1987 (Health and Safety Code Section 44360 *et Seq.*). The act specifies how local Air Pollution Control Districts determine which facilities in the area will prepare a health risk assessment, how such health risk assessments should be prepared, and how the results are to be prioritized. These Guidelines were prepared to provide consistent risk assessment methods and report presentation to: 1) compare one facility against another, 2) expedite the review of risk assessments by reviewing agencies, and 3) minimize revisions and re-submission of risk assessments. The various health-based exposure levels developed for and employed in this program should not be used outside the framework of the program. That is to say, the State of California does not consider them to be general, independent, legally enforceable air quality guidelines or limit values at this time.

5. *Documentation Available:*

CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association (CAPCOA).

Office of Environmental Health Hazard Assessment, 1988. Proposition 65 Risk Intake Levels for Acrylonitrile.

Risk Assessment Advisory Committee, 1996. A Review of the California Environmental Protection Agency's Risk Assessment Practices, Policies, and Guidelines.

Key Reference(s):

US EPA, 1999a. Integrated Risk Information System (IRIS) Database. On-line. US Environmental Protection Agency. Office of Research and Development, Washington, D.C., U.S.A.

O'Berg, M. 1980. Epidemiologic Study of Workers Exposed to Acrylonitrile. J. Occup. Med. 22: 245-252.

OEHHA, 1997b. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

6. Peer Review Process and Public Consultation:

Cancer potency slope factors and acute and chronic reference levels were prepared by the California Office of Environmental Health Hazard Assessment (OEHHA) using peer-reviewed scientific data. Both the exposure and health assessments have undergone public review and comment prior to finalization. Under the CAPCOA risk assessment process, each assessment is site specific and public notice to all exposed individuals is required when the assessment concludes that a significant health risk is associated with emissions from a facility. Public input is obtained in identifying and ranking areas and facilities for risk assessment screening. Further additional input is expected as the process moves forward.

7. Status of Guideline:

The guideline is current, but updates using new California risk assessment evaluations are being considered in the California Senate. Acrylonitrile is regulated under Proposition 65, Title 22, Sec. 12705b. "The cancer potency factors have been used as a basis for regulatory actions, ... and are used in a variety of risk assessment scenarios, including, but not limited to, risk assessments conducted for the Air Toxics Hot Spots Information and Assessment Program and for CERCLA/RCRA programs" (California EPA, 1994).

8. Key Risk Assessment Considerations:

California agrees with the EPA's RfC of $2 \mu\text{g}/\text{m}^3$ as its non-cancer chronic inhalation Reference Exposure Level (OEHHA, 1997b). The toxicological end-points to be considered in the determination of a hazard index are the irritation of the respiratory system and skin, or some other skin effects. Acrylonitrile is also listed as a substance whose emissions must be quantified. A risk assessment of acrylonitrile has been carried out under Proposition 65. California used the upper 95% bound on US EPA unit risk and modified this for a 70 year lifetime exposure, rather than 60 used by the US EPA. This gave an inhalation unit risk of $2.9 \times 10^{-4} \mu\text{g}/\text{m}^3$. This is equivalent to an estimated excess cancer risk of 1 in 10^6 for lifetime exposure to $0.003 \mu\text{g}/\text{m}^3$ of acrylonitrile.

9. *Key Risk Management Considerations:*

The exposure guidelines were prepared for both non-cancer and cancer-based endpoints. The cancer-based value is used in a screening risk assessment to determine the maximum offsite cancer risk for exposed human population. The process is not readily comparable to the air quality guideline approach to non-carcinogens. The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

The State of California allows local options to address the possible economic impacts of emission control. It appears that the options are under local control and are based on local risk, socioeconomic analyses, and feedback from public workshops and hearings. The enforcement mechanism is via operating permits. Thus, the process is primarily directed towards site-specific evaluations and development of further regulatory tools rather than towards enforceable levels in themselves.

10. *Multimedia Considerations of Guidelines:*

In the exposure modelling process, non-inhalation pathways should be considered for a number of substances (specified in Table III-5 in CAPCOA, 1993). Acrylonitrile is not one of the substances requiring non-inhalation modelling. However, the oral unit risk for acrylonitrile is shown to be 1 mg/kg/day compared to the US EPA at 0.54 mg/kg/day, showing the US EPA's value to be 1.9-fold lower.

11. *Other Relevant Factors:*

No information.

11.3 Agency-Specific Summary: State of Massachusetts

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* Commonwealth of Massachusetts

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL; 24-hour average) for acrylonitrile is $0.4 \mu\text{g}/\text{m}^3$ and the Allowable Ambient Limit (AAL ; annual average) is $0.01 \mu\text{g}/\text{m}^3$ corresponding to an excess lifetime cancer risk of 1×10^{-6} .

4. *Application:*

"... The Division of Air Quality Control, which is responsible for implementing the Department's air programs, plans to employ the AALs in the permitting, compliance, and enforcement components of the commonwealth's air program in general, and the air toxics program in particular." (Commonwealth of Massachusetts, 1990, Volume 1, p. ix). The Department of Environmental Protection (DEP) is responsible for developing, among other environmental programs, the air toxics program, the primary objective of which is to protect public health. The limits generated by the program are "health-based only and were developed without regard to production volume, exposure level, or regulatory implication. Similarly, economic and control technology issues are neither discussed nor considered here." (Commonwealth of Massachusetts, 1990, Volume 1, p. 4). Thus, the ambient air levels developed in this process are not to be considered as legally enforceable air standards, rather, they should be employed as guidelines in the development of subsequent regulatory action which does contain a broad consideration of all relevant concerns.

5. *Documentation Available:*

Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, MA.

Office of Research and Standards (ORS), 1994. 1) Revisions to Massachusetts allowable ambient air limits for compounds with inhalation reference concentrations, 2) publication of updated list of Massachusetts AALs and TELs, 3) incorporation of inhalation reference concentrations into the CHEM/AAL process and 4) decisions made by ORS regarding some discrepancies observed in the RfC methodology. Letter from the ORS to the DEP, October 1994, 10 pp.

Massachusetts Department of Environmental Protection (DEP), 1995. Updated list of 24-hour average Threshold Effects Exposure Limit (TEL) values and annual average Allowable Ambient Limit (AAL) values.

Key Reference(s):

US EPA, 1999a. Integrated Risk Information System (IRIS) Database. On-line. US Environmental Protection Agency, Office of Research and Development, Washington, DC.

US EPA, 1983. Health Assessment Document for Acrylonitrile. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park., NC. EPA-600/8-82-007 F. EPA

International Agency for Research on Cancer (IARC). 1979. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 19. IARC, Lyons, France.

International Agency for Research on Cancer (IARC). 1982. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. IARC Monographs, Suppl. 4. IARC, Lyons, France.

American Conference for Governmental Industrial Hygienists (ACGIH). 1986. Documentation of the Threshold Limit Values. Fifth Edition. ACGIH, Cincinnati, Ohio.

6. Peer Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature were employed in the development of these values. Specifically, evidence from the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP) and the US EPA was used. As guidelines, the process used and values generated are not subject to the extensive review and consultation that air quality standards would be subjected to. However, external peer reviews on the Massachusetts methodology and guideline documentation have been carried out and public input was solicited at a minimum of two public meetings on the Massachusetts methodology and guideline document (D. Manganaro, Massachusetts Department of Environmental Protection, personal communication to MOEE Staff). However, in the letter explaining the decision of the DEP to use the available US EPA's RfC values for the corresponding chemicals, no mention of public or any other type of review is mentioned.

7. Status of Guideline:

Current. The DEP estimates that each individual AAL will undergo review at least every three years. In addition, the DEP will re-issue a complete list of AALs on an annual basis in January of each year.

8. Key Risk Assessment Considerations:

Massachusetts uses occupational literature as a database for assessing acute and chronic toxicity of chemicals, and to select a beginning number for use in deriving preliminary human exposure limits for chemicals with threshold effects. The Most Appropriate Occupational Limit (MAOL) is defined as the

occupational limit which provides the best protection against the greatest number of documented health effects. The results of the scoring for acute and chronic health effects is obtained by combining the MAOL with a severity factor according to a scoring matrix. The weight-of-evidence classification for acrylonitrile, for acute and toxic effects as well as animal and human carcinogenicity, places it in Group 'A' as a human carcinogen. Using the EPA's Gene-Tox database as the source of scientifically valid data, acrylonitrile was given a score of 'A' for sufficient mutagenicity on the basis of positive results in bacterial gene mutation assays (*Salmonella typhimurium* and *E. coli*) and positive cell transformation assays (Syrian hamster embryo).

The unit risk value of 6.8×10^{-5} is adopted from the US EPA. The Allowable Ambient Limit (AAL) for acrylonitrile corresponding to an excess lifetime cancer risk of 1×10^{-6} was determined to be $0.01 \mu\text{g}/\text{m}^3$. AALs are based on both threshold and non-threshold health effects and correspond to either the Threshold effects Exposure Limit (TEL) or the Non-threshold effects Exposure Limit (NTEL), whichever is lower.

The 24 hour average concentration of $0.4 \mu\text{g}/\text{m}^3$ was based on the US EPA chronic RfC divided by 5. This assumes that 20% of exposure to acrylonitrile is from air.

9. Key Risk Management Considerations:

The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population. The upper bound unit cancer risk for acrylonitrile is 6.8×10^{-5} . This has been adopted from the US EPA. For carcinogens, a maximum allowable increase in risk associated with exposure to a chemical is set at 1×10^{-6} . The Division of Air Quality Control plans to employ the AALs in the permitting, compliance, and enforcement components of the air toxics program.

10. Multimedia Considerations of Guidelines:

A multimedia exposure adjustment factor of 20% is systematically applied as a relative source contribution factor. The 1994 revision states that the method to derive AALs has not changed. When adequate cancer potency data exist, the approach of applying an uncertainty factor (NTEL) is used to develop a limit based on non-threshold effects. The AAL will then continue to be the lower of the values of the TEL or the NTEL (ORS, 1994).

11. Other Relevant Factors:

No information.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* Michigan (Department of Natural Resources)

3. *Guideline Value(s):*

The screening level (Initial Threshold Screening Level; ITSL) in Michigan is set at $2 \mu\text{g}/\text{m}^3$ using an averaging time of 24 hr.

The Initial Risk Screening Level (IRSL), based on an annual average, is $0.01 \mu\text{g}/\text{m}^3$ which is related to a cancer risk level of one in a million.

The Secondary Risk Screening Level (SRSL) is $0.1 \mu\text{g}/\text{m}^3$ which is related to a cancer risk level of 1 in 100,000.

4. *Application:*

The screening levels are developed for the implementation of Michigan's air toxics rules. These rules apply for permitting purposes. When there is emission of a toxic air contaminant, the best available control technology for toxics must be applied. Furthermore, the maximum ambient concentration of each toxic air contaminant cannot exceed its screening level.

5. *Documentation Available:*

Michigan Department of Natural Resources/ Environmental Quality, 1995/1997. Air Toxics Screening Levels. Air Quality Division.

Key Reference(s):

O'Berg, M. 1980. Epidemiologic Study of Workers Exposed to Acrylonitrile. J. Occup. Med. 22: 245-252.

Quast, J.F., D.J. Schuetz, M.F. Balmer, T.S. Gushow, C.N. Park and M.J. McKenna. 1980. A two-year Toxicity and Oncogenicity Study with Acrylonitrile following Inhalation Exposure of Rats. Dow Chemical Co. Toxicology Research Laboratory, Midland, MI.

US EPA, 1983. Health Assessment Document for Acrylonitrile. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park., NC. EPA-600/8-82-007 F. EPA.

US EPA, 1999a. Integrated Risk Information System (IRIS) Database. On-line. US Environmental Protection Agency. Office of Research and Development, Washington, D.C., U.S.A.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current. An updated list of screening levels that have been revised or newly established is produced every two months while a complete list of all screening levels is published at the beginning of each year.

8. *Key Risk Assessment Considerations:*

When IRSL and SRSL values are established for carcinogens, they are based on the cancer potency values published by the US EPA. If these values are not available, the EPAs HEAST values are used as the basis. If none of these are found, the toxicologist establishes the screening levels using inhalation toxicity data, if available. Michigan uses the same data as the US EPA for the determination of unit risk. The evaluation of the same studies that the US EPA used for its determination of cancer risk (O'Berg, 1980; Quast et al., 1980) were determined to be sufficiently robust (sufficiently large cohort, adjustment for smoking in humans; 2-year rat inhalation and oral studies) for use by Michigan. Acrylonitrile is classified by weight-of-evidence as a probable human carcinogen (B1) in accordance with the US EPA. The unit risk of 6.8×10^{-5} per $\mu\text{g}/\text{m}^3$ was calculated from a relative risk model adjusted for smoking and based on a continuous lifetime equivalent of occupational exposure (Section 11.1).

The US EPA RfC of $2 \mu\text{g}/\text{m}^3$ was adopted for the ITSL. See Section 11.1.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No Information.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* New Jersey

3. *Guideline Value(s):*

The reference concentration for inhalation of acrylonitrile in New Jersey is 2 µg/m³.

The unit risk factor for inhalation of acrylonitrile is 6.8x10⁻⁵.

4. *Application:*

The list of reference concentrations for inhalation are maintained by the Department of Environmental Protection to help in developing a risk assessment for permit purposes. Risk screening, as developed by the Air Quality Permitting Program, consist of two levels. The first risk screening level uses information from permit applications and generalised worst case assumptions to estimate non-cancer and cancer risk from inhalation. Sources which fail the first level screening are submitted to a second risk screening level which uses additional information and a mathematical dispersion model to more accurately predict risk. In the case of sources which fail both screening levels, the Risk Management Committee makes its recommendation based on a case-by-case evaluation. A refined risk assessment is compulsory for certain categories of sources (coal-fired plant, medical, pathological, industrial or commercial incinerators, etc.).

5. *Documentation Available:*

New Jersey Department of Environmental Protection (NJDEP), 1994. Guidance on Preparing a Risk Assessment for Air Contaminant Emissions, Technical manual 1003. Air Quality Permitting Program, Bureau of Air Quality Evaluation, 20 pp. + 7 Appendices.

Key Reference(s):

US EPA, 1993. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The risk screening procedure considers only inhalation exposure. Every source is not modelled individually. Instead, monographs, developed using dispersion models, are used to calculate ambient air concentrations of each source chemical. New Jersey adopted the US EPA RfC (see 7.1). The RfC is to be compared to the maximum annual average ambient air concentration.

In the case of carcinogens, the averaging time is annual assuming ambient exposure levels to the chemical all the time. Long term effects are calculated on the basis of the maximum annual average air concentration. In the case of carcinogens, this latter concentration is multiplied by the unit risk factor to obtain the incremental risk for a chemical. In addition, New Jersey believes that just because a chemical has not shown carcinogenicity, it is not a proven non-carcinogen. The Air Quality Permitting Program (AQPP) assumes a linear dose-response relationship, with no threshold, for carcinogenic substances. The compound is classified as a B1 carcinogen according to the US EPA classification of carcinogenicity. New Jersey adopted the US EPA unit risk factor of 6.8×10^{-5} .

9. Key Risk Management Considerations:

Public health risk estimates of incremental risk for inhalation of carcinogens are calculated as a product of the maximum annual average ambient air concentration of a chemical ($\mu\text{g}/\text{m}^3$) and the chemical-specific unit risk factor ($\mu\text{g}/\text{m}^3$)⁻¹. The AQPP uses this information for its risk management. The policy has the following three guidelines: (1) if the incremental cancer risk is less than 1 in 10^{-6} , the risk is considered negligible, (2) if the risk is greater than 1 in 10^{-4} , the risk is considered unacceptable, and (3) if the risk lies between the preceding two values, the risk is evaluated on a case-by-case basis.

10. Multimedia Considerations of Guidelines:

The risk screening procedure considers only exposure by the inhalation route.

11. Other Relevant Factors:

No information.

11.6 Agency-Specific Summary: State of New York

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* New York State Department of Environmental Conservation

3. *Guideline Value(s):*

The Short-term Guideline Concentration (SGC; 1-h average air concentration) is $220 \mu\text{g}/\text{m}^3$ and the Annual-average-based Guideline Concentration (AGC) is $0.01 \mu\text{g}/\text{m}^3$. Acrylonitrile is classified as a high toxicity air contaminant and is given an "A" 6NYCRR Part 212 Environmental Rating. For compounds with such a rating, the maximum annual average ambient impact is required not to exceed the AGC. Similarly, the one hour short-term SGC must also not be exceeded. "A" rated compounds also require the application of "Best Available Control Technology" (BACT) to achieve 99% or greater pollution control.

4. *Application:*

"... The guidelines ... are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212, 257." (NY DEC, 1991, p. 1). These guidelines are not established as ambient air quality standards but they are intended to protect the general public from adverse effects that may be induced by exposure to ambient air contaminants. These regulations refer specifically to construction and operation (Certificate to Operate) permits for any sources of air contamination. The guidelines are used to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. *Documentation Available:*

New York State Department of Environmental Conservation (DEC), 1991. New York Air Guideline-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation., Albany, New York NY, 20 p. + Appendices.

Key Reference(s):

United States Environmental Protection Agency (US EPA). 1986. Guidelines for Carcinogen Risk Assessment. Federal Register 51: 33992-34003. (9/24/86)

American Conference of Governmental Industrial Hygienists, 1990-1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Ohio, Cincinnati.

6. Peer Review Process and Public Consultation:

The scientific documents prepared by the New York State employed peer reviewed data and models as well as professional judgement of its scientific staff. There are opportunities for public comment on guidelines and the guidelines development process.

7. Status of Guideline:

Current. The New York State Air Guide - 1 is dated 1991. The latest version of the companion Appendix B of the New York State Air Guide-1 is dated April 4, 1994.

8. Key Risk Assessment Considerations:

Acrylonitrile is classified as a high toxicity air contaminant by New York State (1994). This classification includes human carcinogens, potential human carcinogens and other substances posing a significant risk to humans. Classification is based on data from epidemiology studies, the full range of toxicology studies in animals, and a review of the scientific and medical literature. Data from inhalation studies takes precedence over data from studies using other routes of exposure. Particular attention is paid to information on carcinogenic or genotoxic potential. Models using low-dose linearity are preferred unless there is sufficient evidence to support another dose-response extrapolation model. The derivation of the AGC is based on studies with data that show biologically and statistically significant tumour type incidence, duration and route of exposure, as well as, the greatest sensitivity. In the absence of appropriate scientific data the dose extrapolation from animal to human is performed by surface area conversion. New York adopted the US EPA cancer unit risk for its AGC.

New York derived a Short-term Guideline Concentration (SGC; 1 hr) by applying an uncertainty factor to the NIOSH REL-TWA of 1 ppm (2,170 $\mu\text{g}/\text{m}^3$).

9. Key Risk Management Considerations:

Environmental Ratings are reviewed for each contaminant every time a Certificate to Operate comes up for renewal. A specific computer model and guidance manual are provided for use of the guidelines in impact screening analyses to be employed in the permitting process.

10. Multimedia Considerations of Guidelines:

Considers human airborne exposure only.

11. Other Relevant Factors:

NIOSH (1988,1997) notes that since acrylonitrile is a potential carcinogen, the REL-TWA of 1 ppm (2,170 $\mu\text{g}/\text{m}^3$) is based on the lowest feasible concentration.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* World Health Organization

3. *Guideline Value(s):*

The unit cancer risk for a lifetime exposure to $1 \mu\text{g}/\text{m}^3$ of acrylonitrile is determined to be 2×10^{-5} for lung tumours. Acrylonitrile is classified as an IARC Group 2A carcinogen because it is carcinogenic to animals with limited evidence of carcinogenicity in humans.

4. *Application:*

The WHO Air Quality Guidelines are intended to provide a basis to protect public health from adverse effects of air pollution, and to provide background information and guidance to governments in making risk management decisions. However, it should be noted that no standards as such are promulgated by the WHO.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark, 426p.

Key Reference(s):

Delzell, E. and R.R. Monson. 1982. Mortality among Rubber Workers. VI. Men with Exposure to Acrylonitrile. J. Occup. Med. 24: 767-769.

Maltoni, C., A. Ciliberti and V. diMaio. 1977. Carcinogenicity Bioassays on Rats of Acrylonitrile Administered by Inhalation and by Ingestion. Med. Lavoro. 68: 401-411.

O'Berg, M. 1980. Epidemiologic Study of Workers Exposed to Acrylonitrile. J. Occup. Med. 22: 245-252.

Quast, J.F., D.J. Scheutz, M.F. Balmer, T.S. Gushow, C.N. Park and M.J. McKenna. 1980. A Two-Year Toxicity and Oncogenicity Study with Acrylonitrile Following Inhalation Exposure of Rats. Prepared by the Toxicology Research Laboratory, Health and Environmental Sciences, Dow Chemical USA, Midland, MI, for the Chemical Manufacturers Association, Washington, DC.

US EPA. 1983. Health Assessment Document for Acrylonitrile. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC.

Werner, J.B. and J.T. Carter. 1981. Mortality of United Kingdom Acrylonitrile Polymerisation Workers. *Br. J. Ind. Med.* 38: 247-253.

World Health Organization. 1983. Acrylonitrile. *Environmental Health Criteria* , No. 28.

6. Peer Review Process and Public Consultation:

Scientific background documents were prepared by experts and submitted to working groups consisting of international experts to provide a basis for discussion. After a series of meetings and internal and external reviews by experts and representatives of the Member States of the Region, the resultant conclusions and recommendations were presented at a final meeting where they were adopted by consensus of the representatives. In addition, peer-reviewed scientific research data were employed in the development of these documents.

7. Status of Guideline:

Currently applicable.

8. Key Risk Assessment Considerations:

Acrylonitrile showed evidence of mutagenicity in *Salmonella typhimurium*, *Escherichia coli* and *Saccharomyces*. There was also evidence of cell transformation of Syrian hamster embryo cells, sister chromatid exchange in Chinese hamster embryo cells, as well as, in human lymphocytes in the presence of an activation system, and chromosomal aberrations in hamster lung fibroblasts. *In vivo* short-term studies were predominantly negative. Long-term carcinogenicity bioassays in rats showed an increased occurrence of tumours of the central nervous system, Zymbal gland, stomach, tongue, mammary glands and small intestine in both males and females. These results are considered to show sufficient evidence of carcinogenicity in rats.

In humans, both the toxicological and carcinogenic effects of acrylonitrile were examined. The toxicological effects of acrylonitrile were demonstrated by irritation of the eyes, nose and throat, dull headaches, fullness of the chest, itching and nervous irritability. At higher concentrations, vertigo, nausea, vomiting, tremors, convulsions, diarrhoea and jaundice were sometimes noted. Of the twelve epidemiology studies reviewed, only five showed evidence of cancer risk. The studies had some deficiencies in methodology and consideration of major factors in the analysis. On the basis of the results found in these studies, it was concluded that there was limited evidence of carcinogenicity in humans.

The epidemiological study of O'Berg (1980) presents the clearest available evidence of acrylonitrile being a lung carcinogen in humans. 43 cases of lung cancer were reported as opposed to 37.1 expected. The follow-up study (O'Berg, 1985), gave a lower relative risk (R) of 10 (expected)/7.2(observed). Using the assumption of the US EPA (1983) the average lifetime exposure

(X) was calculated as $930 \mu\text{g}/\text{m}^3$. Using the average relative risk model, the unit lifetime risk (UR) for exposure to $1 \mu\text{g}/\text{m}^3$ can be calculated as 1.7×10^{-5} [$\text{UR} = P_0(R-1)/X = 0.04(1.4-1)/930$]. This is similar to the estimated risk of 1.5×10^{-5} derived rat studies by the US EPA (1983).

9. Key Risk Management Considerations:

No information.

10. Multimedia Considerations of Guidelines:

Exposure from air, drinking water and food was considered in the evaluation of acrylonitrile. However, this did not contribute to the determination of the IARC classification or the determination of unit risk.

11. Other Relevant Factors:

No information.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* The Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

The national air limit value not to be exceeded for acrylonitrile is $1 \mu\text{g}/\text{m}^3$ for an annual average with a target value of $0.1 \mu\text{g}/\text{m}^3$. The emission standard is $5000 \mu\text{g}/\text{m}^3$ for a mass flow of 5.0 kg per hour or more. Acrylonitrile is classified as C.3, a non-threshold carcinogen. This classification is defined by the emission concentration of $0.1 \mu\text{g}/\text{m}^3$ which results in an additional cancer risk of 1 in 10^6 with lifetime exposure. This compound is black listed in air, therefore, the target is to have zero release.

Note: Acrylonitrile is erroneously classified as C.2 in Appendix 4 of The Netherlands Emission Regulations. All other data in all the available documentation are consistent with the C.3 classification in Chapter 2.

4. *Application:*

Limit values are non-statutory environmental quality objectives that are considered policy guidelines which should not be exceeded and are requirements that must be met. These effect-oriented guidelines may be used simultaneously with source-oriented emission criteria, which are the primary regulatory mechanism. If effect-oriented guidelines continue to be exceeded, then existing source-oriented emissions criteria will be lowered to bring ambient levels below the effect-oriented guidelines.

The target value is the level at which the risk of adverse effects to the ecosystem, functional properties of the environment or other compartments are considered negligible. The ultimate objective of the environmental quality guidelines of The Netherlands is that the target value might eventually become similar to the limit value.

5. *Documentation Available:*

The Netherlands MHSPE, 1994. Environmental Quality Objectives in The Netherlands. A review of environmental quality objectives and their policy framework in The Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands. 465 pp.

NeR Staff Office, 1992. The Netherlands Emission Regulations - Air. Netherlands Emission Regulation Staff Office, Bilthoven, The Netherlands. 81 pp. + Appendices.

Van de Plassche, E.J. and G.J.M. Bockting. 1993. Towards Integrated Environmental Quality Objectives for Several Volatile compounds. National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands. Report no. 679101 011.

Key Reference(s):

Earlier air criteria documents or more recent integrated criteria documents are available for priority substances, but are only available in Dutch.

6. Peer Review Process and Public Consultation:

No specific information on this issue was presented in the available English documentation.

7. Status of Guideline:

Current. In 1993, recent studies were evaluated and the determination was made that no updating of the information for acrylonitrile was required.

8. Key Risk Assessment Considerations:

Acrylonitrile is considered to be a carcinogen, class C.3, under The Netherlands Emission Regulations on the basis of the Minimum Immission Concentration at which a risk of one extra cancer case occurs per 10^6 given lifelong exposure. The national guidelines issued are derived from occupational hygiene limit values (Maximum Acceptable Concentration, or MAC values) dating from 1992. The national limit values for air are based on extensive risk assessment. The annual average Maximum Acceptable Concentration is $9,000 \mu\text{g}/\text{m}^3$ which is a value used as an environmental hygiene criterion for the workplace. The Maximum Permissible Concentration (MPC) of acrylonitrile in air is $10 \mu\text{g}/\text{m}^3$. No ambient air concentrations were available.

9. Key Risk Management Considerations:

Risk management is carried out by progressive criteria setting. In principle, the target value is set to the negligible concentration or the naturally occurring background value, whichever is higher. A limit value should not be exceeded and a guidance value should be avoided whenever possible. With time, the values are tightened to reach the target value.

Carcinogens without a threshold value are subject to compulsory minimisation under The Netherlands Emission Regulations. Acrylonitrile is black-listed for emission into air in The Netherlands. Substances are placed on this list on the basis of their environmentally harmful properties and not on the risk estimate of the substance. Furthermore, the black list is only relevant to source-oriented policy. The best available means (bam) has to be used to reduce pollution by this substance. Since these substances may occur naturally or may be produced from other countries, the substance(s) may be included on a priority substance list for special attention.

10. *Multimedia Considerations of Guidelines:*

Multimedia exposure was not considered in the development of the current air guideline limits.

However, inter-compartmental criteria which address this problem are being developed. Information is currently available on the MPC and the NC (negligible concentration) of water, soil, sediment and air.

11. *Other Relevant Factors:*

No information

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* Swedish Environmental Protection Agency

3. *Guideline Value(s):*

No guidelines.

4. *Application:*

No information.

5. *Documentation Available:*

Victorin, K., 1993. Health Effects of Urban Air Pollutants: Guideline Values and Conditions in Sweden. Chemosphere 27: 1691-1706.

Victorin, K., 1997. Personal communication.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No information.

11. *Other Relevant Factors:*

No information.

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* Environment Canada

3. *Guideline Value(s):*

Acrylonitrile has been assessed under the second Priority Substance List (PSL2). No specific air quality guideline value has been identified for acrylonitrile. However, cancer risk-based tumourigenic concentrations at 5% increase in incidence (TC₀₅) of 6 mg/m³ and 8.6 mg/m³ based on tumours observed in female and male rats, respectively, have been proposed for acrylonitrile.

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines. Based on the draft document released in July 1999, it is proposed that acrylonitrile be considered "toxic" as defined in Section 11 of CEPA..

5. *Documentation Available:*

Environment Canada, 1999. *Canadian Environmental Protection Act* Priority Substances List Assessment Report (draft) - Acrylonitrile, Environment Canada, Health Canada. Minister of Supply and Services Canada; Ottawa, Canada. February 1999.

Environment Canada, 1999. *Canadian Environmental Protection Act* Priority Substances List Assessment Report (draft) - Acrylonitrile, Supporting Documentation, Health-related Sections (Exposure), Environment Canada, Health Canada. Minister of Supply and Services Canada; Ottawa, Canada. March 1999.

Environment Canada, 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA), Environment Canada, PSL2 Secretariat. October 1995. Also available on the Internet:
www.ec.gc.ca/cceb1/eng/policy_e.htm

Key Reference(s):

Quast, J.F., D.J. Scheutz, M.F. Balmer, T.S. Gushow, C.N. Park and M.J. McKenna. 1980a. A Two-Year Toxicity and Oncogenicity Study with Acrylonitrile Following Inhalation Exposure of Rats. Prepared by the Toxicology Research Laboratory, Health and Environmental Sciences, Dow Chemical USA, Midland, MI, for the Chemical Manufacturers Association, Washington, DC.

6. Peer Review Process and Public Consultation:

CEPA underwent comprehensive public consultation and review. The PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released. Experts from various fields are invited by Environment Canada to participate actively in the assessment process. They form an Environmental Resource Group, which can include scientific and technical experts from all levels of government, industry, academia, environmental groups, and other interested parties. Acrylonitrile assessment report has been released in July 1999 for public review.

7. Status of Guideline:

No information.

8. Key Risk Assessment Considerations:

The inhalation study of Quast *et al.* (1980a) has been chosen as the key source for quantitative data and astrocytoma of the CNS has been considered the most appropriate tumour type for cancer risk estimation (see also Section 3.5). This study was selected because of the size of the groups ($n=100$) and it was a lifetime study (two years of exposure), despite the fact that there were only two doses tested. Both benign and malignant tumours of the astrocytoma type in the CNS were combined for the calculation, using a multistage model (GLOBAL 82). Tumour incidences have been adjusted to exclude animals dying before six months (prior to observation on the first tumour). Dose scaling between animals and humans was considered to account for differences in inhalation volume and body weight, based on the averaged breathing volume of 0.11 m^3 air/day for a 0.35 kg rat and 23 m^3 /day for a 70 kg adult human.

The tumourigenic concentration at 5% increase in incidence or mortality (TC_{05}) for the combined tumour incidence of tumour in the brain and the spinal cord in female rats is estimated to be $6000 \mu\text{g}/\text{m}^3$ ($8900 \mu\text{g}/\text{m}^3$ for the male rats). This is the lowest TC_{05} (human equivalent value). The lower 95% confidence limit is $4500 \mu\text{g}/\text{m}^3$. The application of a margin of safety factor of 5000 and 50000 to the TC_{05} will provide protection to that associated with the range for low dose risk estimates generally considered by various agencies to be "essentially negligible", i.e. 10^{-5} and 10^{-6} respectively (Health Canada, 1996). Thus, at an exposure concentration of $1.2 \mu\text{g}/\text{m}^3$ for a lifetime, the likelihood of tumour incidence is at one in a hundred thousand. This value is in close agreement with the risk specific concentration at an equivalent risk level based on the ED_{10} for female rats as estimated by TERA.

9. *Key Risk Management Considerations:*

No Information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

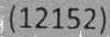
No information.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level</i> (Massachusetts)
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration</i> (New York State)
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	Either <i>Reference Exposure Level</i> as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or <i>Recommended Exposure Limit</i> used by both NIOSH and ATSDR
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumourigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumourigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>



MOE/RAT/AOKV

[illegible]

MOE/RAT/AOKV

Ontario Ministry of the En
Rationale for the

development of Ontario
air standards for acrylonitrile